EXHIBIT D

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

In re: NEURONTIN MARKETING,
SALES PRACTICES AND PRODUCTS
LIABILITY LITIGATION
_____/
THIS DOCUMENT RELATES TO: MDL Docket No. 1629
Bulger v. Pfizer, et al. Master File No. 04-10981
07-11426-PBS

Smith v. Pfizer, et al.
05-CV-11515-PBS
Crone v. California State Court
_____/

The videotaped deposition of SHEILA WEISS SMITH, PH.D. was held on Monday, December 22, 2008, commencing at 9:17 A.M., at the Law Offices of Goodell, DeVries, Leech & Dann, LLP, 20th Floor Commerce Place, One South Street, Baltimore, Maryland 21202, before Ronda J. Thomas, a Notary Public.

Job No.: 183061
REPORTED BY: Ronda J. Thomas, RPR, CLR

APPEARANCES:

ON BEHALF OF THE PLAINTIFFS, PRODUCTS LIABILITY
STEERING COMMITTE AND CRONE:
KEITH ALTMAN, ESQUIRE
Finkelstein & Partners
436 Robinson Avenue
Newburgh, New York 12550
Telephone: 845.562.0203
Facsimile: 845.562.3492
Email: Kaltman@lawampmmt.com

ON BEHALF OF PFIZER AND MDL:
RICHARD M. BARNES, ESQUIRE
MICHAEL J. WASICKO, ESQUIRE
Goodell, DeVries, Leech & Dann, LLP
One South Street, 20th Floor
Baltimore, Maryland 21202
Telephone: 410.783.4000
Facsimile: 410.783.4040
Email: Rmb@gdldlaw.com, mjw@gdldlaw.com

(APPEARANCES continued on next page.)

(APPEARANCES continued.)

ON BEHALF OF RAYMOND JENNINGS, M.D.:
ELANA GOLD, ESQUIRE (via teleconference)
Law Offices of Steven D. Hillyard, APC
345 California Street, Suite 1770
San Francisco, California 94104
Telephone: 415.334.6880
Facsimile: 415.334.6967
Email: Egold@hdmlaw.com

ALSO PRESENT: Robert Kowalchik, Videographer

INDEX
Deposition of SHEILA WEISS SMITH, Ph.D.
December 22, 2008

P R O C E E D I N G S

(Whereupon, documents were premarked as Deposition Exhibit Number 18, 19, 20 and 21.)

THE VIDEOGRAPHER: We are on the record. The time is 9:17 a.m. My name is Robert Kowalchik of Nationwide Video Production. The date today is December 22, 2008. This deposition is being held in the office of Goodell DeVries located at One South Street, Baltimore, Maryland.

The caption of the case is in Re: Neurontin Marketing Sales Practices and Products Liability Litigation in the United States District Court, District of Massachusetts. MDL Docket No. 1629 Master File No. 04-10981.

This document relates to Bulger v. Pfizer, et al. 07-11426-PBS and Smith v. Pfizer, et al. 05-CV-11515-PBS and cross noticed in the case of Crone v. Pfizer.

The name of the witness is Sheila Weiss Smith. At this time the attorneys will identify themselves and the parties they represent, after which our court reporter, Ronda Thomas of Doerner and Goldberg, will swear in the witness and we can proceed.

MR. ALTMAN: Keith Altman on behalf of Finkelstein & Partners for the Plaintiffs Products

since this case has been noticed in the Crone matter, we are not under the same time constraints as in the federal MDL which allows for two days of seven hours. We have scheduled one day. I will do everything in my power to conclude my examination in the one day of seven hours but reserve the right to adjourn the deposition and complete it at a later date if I'm unable to do so.

MR. BARNES: I do not believe that the California deposition notice provides you the leeway you seek but as to time we'll take it up at a later date. Why don't you begin.

MR. ALTMAN: Okay.

EXAMINATION BY MR. ALTMAN:

Q Dr. Weiss Smith, before we begin I've marked -- we're continuing the numbering from your last deposition, which was I believe in January of this year, 11 months ago, the deposition exhibit numbering, starting with no. 18.

I'd like to hand you what I've marked as Exhibits 18, 19, 20 and 21 which I'd like you to take a quick look at to see if they are, in fact, your supplemental report, your materials considered and your CV as well as the materials considered from your original deposition.

Liability Steering Committee, as well as the Crone Plaintiffs.

MR. BARNES: Richard M. Barnes on behalf of Pfizer and MDL in the Smith and Bulger cases as well as the Crone case in California.

MR. WASICKO: This is Michael Wasicko from Goodell DeVries on behalf of the Pfizer Defendants.

MS. GOLD: Elana Gold for Raymond Jennings, M.D., in the case of Crone versus Pfizer.

Whereupon,

SHEILA WEISS SMITH, PH.D.,

called as a witness, having been first duly sworn to tell the truth, the whole truth, and nothing but the truth, was examined and testified as follows:

THE VIDEOGRAPHER: We're on the record. The time is 9:21 a.m.

EXAMINATION BY MR. ALTMAN:

Q Dr. Weiss Smith, how are you today?

A Fine, thank you.

MR. BARNES: Counsel, before you begin, I think we all agree that this deposition is not only Smith and Bulger but is applicable to all pending cases in the MDL.

MR. ALTMAN: I think we're in agreement on that. One other thing I want to put on the record

A That looks right.

Q By that you mean Exhibit 18 and your supplemental report, correct?

A Yeah, Exhibit 18 looks like it's the same as what I have. Exhibit 1. Exhibit 19 is the same as what I have, yes. The supplement.

Q By Exhibit 1 you mean what I've marked as Exhibit 19 which is a list of materials considered marked as Exhibit 1 to your supplemental report, correct?

A Exhibit 1 materials considered you wrote Deposition Exhibit 19.

Exhibit 20 is a short CV.

Q That is your current CV; is that correct?

A Yes, it's my short CV.

Q That was provided as part of your supplemental report, correct?

A Was it a part of my supplemental report? I believe so.

MR. WASICKO: Yes.

A What's 21?

Q 21 is, I believe, your materials considered from your original expert report from December of last year.

(Witness reading.)

A Yes. A lot of work. Yes. That is correct.
Q In preparation of your deposition for today, what materials did you review to prepare for this deposition? And I don't mean for creating your expert report. I mean specifically getting ready for today's deposition. Strike that.
When were you first notified of today's deposition?
A Earlier this month.
Q Okay. What did you do from the time you were notified of your deposition today and today in preparation of your deposition?
A Can you narrow that question? What do you want.
Q What did you do to prepare for today's deposition between the time you received notice of the deposition and today?
A Went over my report. Went over the FDA analysis, reviewed some of the materials that are in here. Just --
Q Did you meet with counsel at all?
A Yes, I did.
Q How many times?
A Once or twice.

report?
A Same thing. Nothing substantive. No.
Q Have you ever spoken to anybody in preparation for your reports -- either the original or the supplement report. Have you ever had any conversations with anybody from Pfizer specifically to the topic of Neurontin or anything that is the subject of your expert reports?
A No.
Q Your list of materials reviewed there, I believe they're marked as exhibits -- as exhibits -- is it 19 and 21? Does this contain all of the materials that you reviewed in preparation of this expert report?
A Yes, I believe it does.
Q Did you ever request any materials from -- you say you had no direct contact with anybody from Pfizer, so any materials you received or would have asked for would have been through counsel, correct?
A That is correct.
Q Were there any materials you specifically requested from counsel either in preparation of your supplemental report? Just so we don't have to say it every time. When I say your report, it means your supplemental report or your original report, if there's something specific to one I'll draw the distinction.

Q About how much time did you spend with counsel?
A Not much. We met a couple days ago. Friday, we met Friday. Then I don't know if we met before I went to Taiwan. Did we meet before? I don't think so.
Q Did you talk with anybody from Pfizer in the intervening period?
A Did I speak with anyone from Pfizer? Yes.
Q Who did you talk to from Pfizer?
MR. BARNES: About this deposition.
A Oh, about this, no, of course not.
Q I meant in relation to preparing for this deposition?
A Oh no, no. Just business.
Q You say you've reviewed your report. Are there any -- is your report accurate? Are there any corrections you would like to make to your supplemental report at this time?
A I think I found a typo this morning, but otherwise no.
Q Nothing substantive?
A Absolutely not.
Q When you reviewed your original report, are there any changes you want to make to your original

So in preparation of either of your reports, did you ever request anything, any documents of counsel?
A Yes.
Q What documents did you request?
A I had requested for them to let me know if Pfizer had a waiver for reporting periodic reports, individual periodic reports. And I mentioned that in my report.
Q Okay.
A I asked them to tell me that. I might have -- I think I asked them to see if they could track down a couple of articles in the literature --
Q Okay.
A -- that I couldn't get ahold of. And I kept asking them if the FDA came up with anymore material, if they had heard anything. That's it.
Q Now, as part of your original report, were there any materials you asked for?
MR. BARNES: If you recall.
A I think the only thing I recall is asking, again, for some literature.
Q Okay. There's a lot of literature listed on your materials considered.
A Yes.

Q Did you do all of that research yourself or was that all literature that was provided to you by counsel?
A A lot of it is what I found in the literature and I did literature searches and I would ask them for material.
Q Okay.
A Some I pulled myself but I asked them to do the leg work.
Q Was there literature provided to you by counsel on their own? They just gave you here's some literature you might want to review for example?
A Yes.
Q Did you ask for any company documents to review? Do you understand what I mean by company documents?
A Yes. None that I recall.
Q Were you aware that something on the order of between 2 and 3 million pages of documents were produced by counsel to plaintiffs in this case as part of the document production?
A Excuse me?
Q As part of the document production?
A I don't believe I'm aware of the total number, no.

Q Were you aware that a large number were produced to plaintiff's counsel?
A What's a large number?
Q Did you know that -- did you know that defendant's counsel in this case produced a number of documents to plaintiffs?
A I would assume so.
Q Do you have any idea how many documents were produced to plaintiffs?
A No.
Q Are you aware whether those documents were available on a hard drive?
A What documents?
Q The documents that were produced by counsel to plaintiffs. Were you aware that those were available on a hard drive?
A I'm not quite sure what you're talking about.
Q Are you aware that defendants produced a number of documents to plaintiffs, correct?
MR. BARNES: She said she assumed so.
Q You assume so?
A I would have to assume that. I'm not privy to what's going on between the plaintiffs and the lawyers.

Q So you were not provided with a hard drive of documents representing substantial -- all or most of the document production in this case, were you?
A I don't know what subset of documents I was provided.
Q How did you receive the documents provided, produced to you by counsel?
A I believe they handed them to me, they mailed it to me, or they e-mailed it to me. Depending on what it was.
Q Do you have any idea what volume of material, how many boxes?
A I believe it's all here.
MR. BARNES: We produced -- in the original deposition we produced the boxes of documents that she had -- in response to the original deposition notice that were available at the first deposition. That was covered at the first deposition by Mr. Fromson as to what she had.
So I think what she's prepared to speak about is the supplemental report. The question as to historically what was done last year, that was amply covered. We had the opportunity to cover it regarding the first report.
I would ask you to focus on the

supplemental report because she's not prepared to address the substance of the earlier report. Especially the questions that were discussed with Mr. Fromson last January.
So if you want to focus on the supplemental report I think she's much more prepared to talk about that as to the materials she would have considered and relied upon.
Q Notwithstanding counsel's objection, I point out that -- we'll discuss this later -- you say in your report, I also offer opinions regarding Pfizer's conduct in the development, testing and labeling of Neurontin which were not part of my general causation opinions in my first report --
MR. BARNES: As set forth in her report, counsel. As set forth in the report.
Q Correct. Which means you would have reviewed some of the materials originally produced to you?
MR. BARNES: That may or may not be the case. You might want to establish that first. I don't believe that's the case. I think you're assuming things. Lay a foundation first.
Q Notwithstanding anything, you were not given a hard drive? You do know what I mean by a

computer hard drive, correct?
A Yes.
Q You were not given a hard drive of documents in this case; is that correct?
A That is correct.
Q If you took all of the materials and you printed it out, do you think you had 10 boxes of materials, is that the order of magnitude in terms of documents you received?
A To tell you the truth I don't know. I didn't print things out. I kept most of them on disk.
Q Is that how most of the materials were provided to you?
A Some on hard copy, some on disk, some e-mailed.
Q What materials did you bring with you today to this deposition?
A What is -- I believe it's what is listed on materials considered for the supplemental report.
Q Was that in paper or was that electronic?
A Yes. Some each.
Q We'll take a look at that stuff on a break. Do you have copies of the disk, whatever, for me?
MR. WASICKO: Yes.
MR. ALTMAN: Okay.

Q I notice in your report that you adopt the opinions of Dr. Robert Gibbons; is that correct?
A That is correct.
Q Have you done any independent review of any of the underlying materials that form the basis of his opinions?
A What do you mean by underlying materials?
Q Have you reviewed -- he did a -- he did various pharmacoepidemiologic studies within his expert report. Did you, yourself, review the underlying data that he used in doing those studies?
A Yes and no.
Q Could you explain, please.
A I did look at -- it's in my report, the AERS data and the sales data for Neurontin, that's in my first report. And some of my subsequent report, which is the same data he used for his signal detection work.
On the other one, where he does pharmametrics study, I did not have access to the pharmametrics raw data, but I did have access to the full draft of the manuscript. So I did read that.
Q So in other words you read the manuscript and for example if there was an error in the manuscript, you did not have any independent way of

verifying whether there was an error or not. You're relying upon Dr. Gibbons to have been correct in his manuscript; is that right?
A I rely on evaluating the study that he did.
Q But if he made a mistake in his underlying data analysis or computations or anything like that, you, yourself, did not do anything to verify his work, correct?
A I did not repeat his analysis. I read the paper.
Q Okay. And so your opinions in adopting it are obviously limited by the accuracy of his opinions, correct?
A The accuracy of his opinions?
Q Yes. If his opinion is wrong because he did something wrong with the data analysis, then you've just simply adopted his erroneous opinion of erroneous data analysis?
MR. BARNES: Objection. Assumes facts not in evidence. You may answer.
A You're taking a leap that I don't understand.
Q Okay. We'll move on.
From the time we took your deposition in January, when was the next time you did anything with

respect to this case?
A I was given documents as they came in so I would read things over the months. You, I believe, have my invoices. So over the last year I've read things. Then when the FDA report came out, I read that. Then just preparing, preparing for this deposition.
Q When did you begin preparing the supplemental report?
A When did I begin? I believe it was a few months ago. Maybe in September.
Q So between January and September your activity was basically just reading materials as they came in and everything like that?
A Excuse me?
Q Was just pretty much reading materials as they came -- new materials as they came in, correct?
A That's correct.
Q You were not, let's say, doing substantive analysis of information or research or anything like that? It was mostly responsive to those materials, correct?
A Responsive?
Q Yeah, you were just pretty much reviewing materials as they came to you. You weren't doing your

own active research in that period of time, were you?
A That's correct.
Q In terms of working with the AERS data with respect to this case, did you do any work with the AERS data either on your own or through Q Scan between the time we took your deposition in January and when you began working on this supplemental report?
A I'm continuously doing analysis in the AERS data.
Q For this case?
A For this case.
Q For Neurontin?
A Not specifically for this case.
Q For anything involving Neurontin?
A I've been working in the AERS data. Neurontin is one of the drugs. I did look generally at suicide.
Q When you say generally at suicide, what -- when did you do that?
A Over the past year.
Q Did you do any of that analysis between January and September when you started working on your supplemental report?
A I may have. I've been working pretty continuously on AERS and trends and AERS reporting.

MR. BARNES: She, just to be precise, on her own professional work she is constantly in AERS. Some of the stuff -- almost all the time I'm assuming, your questions are open-ended. You've not been precise as to on behalf of Pfizer or counsel or on behalf of your other professional work.
So objection as to the -- your question is vague as to scope.
MR. ALTMAN: Well, when I ask Neurontin, I mean Neurontin whether in this case or any other context. So specific --
Q I understand that you use AERS every day.
A That's what I'm trying to tell you.
MR. BARNES: You're asking very broad questions and I'm going to start jumping in because I think your questions are very broad. I just want to make sure you understand what he's asking. So go ahead. I think you do now. So go ahead.
THE WITNESS: Thank you.
Q I haven't seen your invoices yet but do you have a ballpark idea what you billed in the interim between January and when you started working on the report?
A Ballpark from January?
Q From after the deposition?

A I do have the invoices. I never did add them up.
MR. BARNES: The answer is, do you have a ballpark? If it's yes or no.
A No, I don't have a ballpark.
Q That's fine. We'll look at -- we'll look at that later.
When you wrote both reports, did you use the same scientific vigor as you would use if you were submitting these reports for publication in a scientific journal?
A They're totally different purposes. But I -- that's what I was hired to do is to look at the science.
Q I understand that. But when I mean scientific vigor, I mean checking citations, checking batch error, math is accurate, checking your charts to make sure that they're accurate. Being sure that, you know, all of those things -- those are the kinds of things you would do if you were submitting a paper to a journal, correct?
A If I was submitting a paper to a journal, yes.
Q Did you do those same things here?
A Not to the same degree checking references

and verifying. I didn't have as many hands, but yes, I made sure that my analysis was right and the numbers that I put in are correct, yes.
Q Is it important that your references are correct in a scientific paper?
A Yes, it is.
Q Is it important in your reports here that your references would be correct?
A Yes, it is.
Q What would happen if your references -- what are some of the consequences of not having accurate references?
A Excuse me?
Q What are some of the consequences of not having accurate references?
A In what context?
Q For somebody who is reading your -- reading your scientific paper or reading these expert reports?
A Well, in the scientific paper it goes through editorial process and it goes through a number of hands. So it would be corrected.
MR. BARNES: She's saying the editorial process in scientific journals is not the same as with here to be precise. Go ahead.
Q If somebody were reading your paper and you

cite to a reference, when I say your paper, I mean your expert reports here, and you cite to a reference and that reference was not correct, they could be led to believe that a reference -- a particular reference may have said something that's in your report that they didn't actually say, correct?

MR. BARNES: Objection. Vague calls for speculation.

A I don't know what they would assume.

Q If you put a -- if you put a statement in your expert report --

MR. BARNES: The supplemental or the original?

MR. ALTMAN: In either report. This is a general concept.

Q If you put a citation in either one of your reports and you put a sentence there and after you put Joe Smith and the name of an article and the, you know, the journal and the citation to that article, you are telling a reader that that is where that citation -- that statement came from, correct?

A You're attributing it to somebody, yes.

Q And if that citation was incorrect, wasn't that person who said it, you could lead somebody reading your report to believe that one person said

A I have no expectations of how it's going to be used. That's up to the lawyers.

Q Do you have an expectation that readers of your reports will sit and review every single one of your references in there to see if they're actually correct?

A I don't know what they're going to do with the report.

Q But you were -- when you put a reference in there, you were intending to tell the reader that that's where that particular statement came from, correct?

A Yes, to properly give attribution to the person who made that finding.

Q And would it be misleading if that particular person didn't actually make that statement?

MR. BARNES: Objection. Calls for speculation and legal conclusion, you may answer.

A I believe and I went through everything to make sure I properly attributed the correct person to the statements that are in there and that I accurately reflected what was in the reference.

Q And if you put a -- you attribute something to a reference and that information is not contained anywhere in the reference, could that mislead a reader

this when it isn't true that they actually said that, correct?

A I don't believe that's how people interpret.

Q What's your belief of how people -- when somebody reading your expert reports would interpret when you cite to a particular author, paper, et cetera?

MR. BARNES: If you know.

A I don't know what people assume. When I see something I -- that I can't find it, I assume that it's a typo or something. I might go and look if I need to find the original reference or I might contact the author and ask them if I can't track it down myself.

Q Did you have an expectation that anybody reading your -- well, strike that.

Do you have an understanding that your expert reports here will be used and reviewed by other experts within this case?

A I believe so, yes.

Q Do you have an understanding that this will be -- and reviewed by attorneys in this case?

A Obviously it was, yes.

Q Do you have an expectation that the court may review your expert report here in this case?

that the reference actually said that?

MR. BARNES: Objection. Calls for speculation.

A Could you show me what you're referring to?

Q I'm just asking as a general concept?

MR. BARNES: If you have an opinion on that, you can answer. If you have no opinion, that's fine, too.

A I don't want to speculate.

Q Do you know overall about what your billings were since January, not necessarily for any given time, just once again general ballpark?

A It varied by month. I never added them up. I haven't done my taxes yet.

Q You say you never spoke with anybody at Pfizer related to this particular litigation; is that correct?

A That is correct.

Q Are there people at Pfizer in which you regularly interact with outside of the context of this litigation but within the areas of your expertise?

A What do you mean regularly?

Q Are there individuals at Pfizer that you correspond with, communicate with, speak to regarding areas of your expertise?

A Yes.
Q Who are they?
A One of the people I know is Manfred Hauben at Pfizer. Lester Reich I know less so. I believe Bob Reynolds also works at Pfizer, I believe.
Q Have you ever spoken to Dr. Hauben about Neurontin?
A No. We specifically do not speak about it.
Q Do you consider yourself an expert in pharmaceutical product labeling?
A An expert?
Q An expert?
MR. BARNES: Would you repeat the question?
Q Do you consider yourself an expert in pharmaceutical product labeling?
A I am knowledgeable about labeling, but I am not one of the preeminent experts in labeling, no.
Q What is the basis for your -- strike that.
In your research do you hold yourself out as somebody that people should go to if they have questions about pharmaceutical labels?
A On the epidemiology and pharmacoepidemiology that's put into the labels on issues that -- that type of issue, so yes, to that extent. The science that I work on as it goes into the

MR. ALTMAN: No. Outside of that -- outside of the FDA.
MR. BARNES: Outside of your work with the FDA, have you corresponded with the FDA about labeling?
A That hasn't been my position to be the correspondent. I worked and advised the FDA and I've worked for companies that have been working on labeling issues, but I'm on an advisory role, not as a person that would be the contact person.
Q And I think you said your advisory role is limited to epidemiology and pharmacoepidemiology issues?
MR. BARNES: As it relates to label.
Q With respect to labeling?
A As it relates to labeling, some organ risk management. So I'm using the broad drug safety issues.
Q But they would all have in commonality, they would be epidemiologic or pharmacoepidemiologic issues, correct?
A Based on those issues, yes.
Q Have you ever reviewed a label to decide whether the label had a -- was accurate from a clinical perspective?
MR. BARNES: What do you mean by clinical perspective?

label.
Q You're not a clinician?
MR. BARNES: Are you finished your answer?
A But I think that's where I'm narrowing it to that. So not the whole label. I also did a lot of work in pregnancy registries and the labeling for drugs and pregnancy.
Q Okay. You're not a clinician, correct?
A That is correct.
Q Have you ever written a pharmaceutical label from scratch?
A No, I have not.
Q Have you ever written any portion of a pharmaceutical label?
A No.
Q Have you ever corresponded with the FDA concerning a label?
A What do you mean by corresponded?
Q Have you ever, in any of your work, have you ever been responsible for corresponding with the FDA about the adequacy of the label or whether a label needs to be changed or anything concerning a product label?
MR. BARNES: Does your question concern her work on Pfizer committees as well to correspond --

Q To a doctor?
A Isn't it all the same thing?
Q No, it's not all the same thing.
MR. BARNES: Objection. Assuming facts not in evidence. Vague.
Q Are you qualified to take a look at a label and decide whether the label accurately represents all of the -- all of the risks known about the product?
MR. BARNES: Objection.
A I'm not sure any one person can know if one label has every single thing in there. Those labels are huge and there's not one person with all the expertise.
Q Have you ever written to the FDA suggesting the labeling change?
A No, I don't typically write to the FDA.
Q Have you ever been part of a group assessing whether a label should be changed?
A Yes, I have.
Q When was that?
A On a number of occasions I have served either on an advisory committee or worked as a consultant to the FDA. On a couple occasions for companies dealing with particular risks and risk management programs. So I've worked on both sides

consulting with them about the risks.
Q Do you know about how many times you've done this? And I don't mean, like, I'm not asking you if a project involved, you know, 20 different interactions. I mean, let's break them up into projects. Do you know about how many projects you worked on in that capacity?
A Probably about a dozen.
Q When you were on the advisory committee, how many of those products involved you being on the FDA advisory committee?
A I probably been on about six or eight advisory committees.
Q When you were on the advisory committee -- were you ever on the advisory committee for the approval of a product?
A Yes, I was.
Q Which products?
A The most recent one, which was before I started on this case, was a -- it was a antiviral drug, it was a Pfizer antiviral drug, Maraviroc.
Q Okay. Before that?
A Before I started any of this.
Q And before that?
A MT100.

Q Which is?
A Which was a combination product for migraine. Never got a name, I believe.
Q What was the chemical compounds?
A I can't remember. There were two drugs that were already approved.
Q Before that?
A I know I was on the committee for Clozapine to look at the monitoring.
Q Do you consider yourself to be a regulatory expert? When I mean regulatory, I mean pharmaceutical regulatory?
A To some extent.
Q What is the basis of that expertise?
A I did a post doctoral fellowship at the FDA in pharmacoepidemiology in regulatory sciences. We took courses taught by regulatory experts at the FDA. I worked there a total of two and a half years and I continually study the FDA process, regulatory process --
THE COURT REPORTER: Please keep your voice up.
MR. BARNES: Yes, you have to keep your voice up.
A I'm sorry -- and I continually work within

the FDA regulatory processing and continue to monitor and study it.
Q Have you ever worked in regulatory affairs for a pharmaceutical company?
A No, I have not.
Q When you were at the FDA in your fellowship that touched upon regulatory issues, what did you do in terms of regulatory affairs at the FDA?
A In addition to taking courses I worked on the guidance documents. So developing guidance for industry. Guidance for FDA medical reviewers. I taught at their staff college on the use of these regulatory guidance and methods, particularly in the drug use in pregnancy issue, reproductive toxicology. Other issues at FDA for regulatory affairs.
Q While at the FDA did you ever review the regulatory activities of a pharmaceutical company?
MR. BARNES: Objection. Vague as to regulatory activities.
Q Strike that. I'll ask it.
Did you ever correspond with pharmaceutical companies on regulatory matters while you were at the FDA?
A I never corresponded directly.
Q Did you correspond indirectly?

MR. BARNES: Are you asking if some of the work she did at FDA was used by others at the FDA in drafting and preparing regulatory correspondence with pharmaceutical companies? Your questions are very vague.
A I'm not quite sure I understand what you're asking me.
Q While at the FDA did you ever work on specific projects that you knew were involved in a particular pharmaceutical company?
A All the projects we worked on at the FDA dealt with the regulated products.
Q I understand that. But were you aware -- when you were at the FDA were you working on a particular -- let's ask a couple different questions.
Have you ever been involved in the review of a new drug application, outside of the context of an advisory committee?
A I might have worked on things at the FDA, but I don't recall anything specific right now.
Q And to be clear with one thing in terms of an advisory committee, the advisory committee does not actually review the massive several hundred thousand page submission from a manufacturer, correct?
A We get a lot for the advisory committee.

But I don't believe we get the full original submission.

Q You typically get -- my understanding is you get a number of reviews that would be done by FDA staff members, a clinical review, a medical review, a statistical review, a toxicology review, et cetera; is that correct?

A That's the one side. But we also get documents from the company directly. So both the FDA and the company submit documents to the advisory committee to review and it's all available on the web.

Q Sure. But they're typically summaries of the material. You're not reviewing -- you're not reviewing all of the detailed case report forms for, you know, clinical trials; is that correct?

A It's typically the summary. Often there will be case report information on there for particular events that they're of concern.

MR. BARNES: So -- did you finish your answer?

A So it's a combination of summary data but also some of the key individual cases, yes.

Q So I understand what you're saying, you've never actually taken -- received the massive volumes produced by a pharmaceutical company and had

considerations that need to be taken when using AERS data that do not require clinical expertise; is that correct?

MR. BARNES: Objection. Assumes facts not in evidence. You may answer.

A There's a lot of clinical issues with the coding of the drugs and the coding of the events that I believe requires clinical expertise. So it would take a phenomenal amount of time and effort to truly clean the data to the point that it needs to be cleaned to use it for research.

Q Are you aware that you cannot get the narratives through the AERS download? And AERS is A-E-R-S. Through the AERS download?

A The FOI information does not include narratives. That's correct. Though you can request them.

Q Can you request them in bulk for all reports?

MR. BARNES: Take your time. You guys are right on the edge of each other. Finish your answer completely. He jumps right in at the end of your answer. I'm not saying he's cut you off. He may be cutting you off so if you guys will just slow it down a bit. Finish your answer and you can ask your next

responsibility for reviewing any portion of the raw volumes as submitted by the manufacturer; is that correct?

A That is correct.

Q Do you consider yourself an expert in pharmacology?

A No.

Q Do you consider yourself an expert in computer databases?

A I'm not a computer programmer, if that's what you mean.

Q Okay. Do you have the technical capabilities to download the FDA AERS data?

A Yes.

Q Do you have the technical capabilities to load that into some kind of a database tool?

A Of course.

Q Do you have the technical capabilities to clean the data, link it together because it's spread in multiple different tables?

A I believe you can't truly clean that without clinical expertise because of the way that the drugs and the events are coded. So that's an issue.

Q But when I say clean, I mean just clean from an objective manner. There are obvious

question. Go ahead.

A Will you repeat that, please.

Q Is it possible to get the AERS data in bulk, including the narratives? Do you know what I mean by when I say in bulk?

A No.

Q You can request for specific report numbers the full MedWatch forms including the narratives, correct?

A I'm aware that you can request them.

Q Can you say to the FDA I'd like the entire AERS database including the narratives?

A They do not release the entire database of narratives from my understanding.

Q And you would need those narratives in order to review the accuracy or adequacy of the coding within the AERS database, correct?

A That's very broad. I don't think I can agree with that.

Q With each adverse narrative report there's a number of adverse event terms associated with it, correct?

A There can be as little -- or as few as one and right now currently can be infinite.

Q And somebody decides what adverse event

terms to assign to a particular report, correct?
A Somebody codes them, yes.
Q And they do that based on the narrative information, et cetera, correct?
A Not necessarily.
MR. BARNES: Objection.
Q What information would they use to do that that's not part of the narrative?
A There are actually a field for adverse event terms.
Q I understand that, but in deciding what adverse event terms to assign to a report, somebody has to review the narrative information for that report, correct?
A If there is a narrative. Not all reports have narratives.
Q Are you talking about in the AERS database or at the ultimate -- the original source of the data that goes into the AERS database?
A The original source data. Not all of it has narratives.
Q Okay. How does somebody decide what terms to assign to a particular adverse event report?
MR. BARNES: Say it again?
Q How does somebody decide what terms to

assign to an adverse event report?
MR. BARNES: Objection. Vague. Calls for speculation and you can answer what your understanding of the process is. Go ahead. Do you understand the question?
A It's huge. I don't think I can go into the protocol.
MR. BARNES: If anyone knows how a specific person codes is a little bit broad.
A Hopefully they're trained and they're accurately reflecting what's in the report.
Q And the report contains some kind of narrative information as to what happened to this person, correct, some kind of a description of what happened; is that correct?
A It's my understanding that not all reports contain narratives.
Q For a report that doesn't contain a narrative, do you have any idea what the source of the adverse event terms would be?
A There's a field that says what were the events that happened, what are you reporting. That's separate from the narrative.
Q So is it your understanding that somebody would decide what terms to use without knowing anything

about the report?
A I don't make any assumptions on who fills in what and why.
Q Did you review Pfizer's procedures for submitting adverse event reports to the FDA?
A No, I did not.
Q And I think I asked you this the last time, you were provided a disk of the ARIS G database, correct?
A Yes.
Q As of the last time you had not actually reviewed the ARIS G data; is that correct?
A I looked at the -- I opened the cases.
Q You looked at it briefly, you opened it up --
MR. BARNES: Objection. Let her finish her answer. You're jumping on her, Counsel. You need to make sure you're finished your answer and then he'll ask you a question. You're not doing anything wrong. He's jumping on your answer. But go ahead.
A Yes, I have the disk. I believe it's in this box and I've looked at the case reports.
Q When you say you've looked at the case reports, what do you mean there?
A Reports in the ARIS G database. I've

looked at the reports.
Q There are something on the order of 100 tables of data within the ARIS G database. Did you actually look at those individual tables to put a case report together or were the case reports provided to you kind of as a completed report?
MR. BARNES: Objection. Assumes facts not in evidence. You may answer.
A I had both. I had the original data tables, which I looked at and I also had reports pulled from that in a summary of reports.
Q So that's something different that you didn't have the last time; is that correct?
A The summary, that is correct.
Q Have you ever done anything other than briefly glance at the tables with respect to the original ARIS G database produced to you?
MR. BARNES: Counsel, if you're going to modify her prior testimony with modifiers, I wish you would use her statements and not your qualifications. You're not accurately summarizing the prior answers. If you're going to do that, you should do it accurately or not at all.
Would you please reask the question.
Q Did you do anything with the original ARIS

G database other than open it up, take a brief look at it?

MR. BARNES: Objection. You may answer.

A I did nothing more with it than I had stated in the original deposition.

Q Do you know what the source of the adverse event report you were asked to look at? What I mean was, were they a -- strike that.

You received an additional disk that had case reports, correct?

A Yes.

Q Did you ask for that disk?

MR. BARNES: If you recall.

A I can't recall. I got so much stuff. We were going back and forth. So I don't know.

Q Okay.

A Within the context why I got that.

Q Were there any particular reports, are they all of the reports, are they a subset of the reports?

A What I saw was a subset of reports that are the suicidality. So the completed suicide, suicide attempt.

Q Did that also include suicidal ideation?

A I don't recall.

Q For the purposes of this -- strike that.

Q Are you familiar with the concept within the FDA AERS database of last best case?

A Yes.

Q What does that mean to you?

A The most current and most complete case. So if there are follow-up reports, it's the report that has the most current and complete information in the series.

Q So does that mean that the FDA database contains more than one version of an adverse event report?

A What do you mean?

Q Does the FDA AERS data contain multiple versions of a particular adverse event report?

A What do you mean versions?

Q When a report is first -- let's just say from a manufacturer to the FDA. When the manufacturer first submits a report to the FDA, that's version 1. Six months later they get some new information about that particular report and they send a revision to the FDA; is that correct? Or may send a revision to the FDA?

A Are you talking about follow-up reports?

Q Follow-up report.

A Okay. There may be follow-up reports. If

I understand that you use the Q Scan system for your AERS analysis; is that correct?

A Q Scan FDA, that's correct.

Q Do you do --

MR. BARNES: You have to keep your voice up.

Q Do you have the FDA data in your own database?

A I have some of the FOI AERS data on my computer, if that's what you mean, subset of it.

Q What do you have that data in? Is it in a database program?

MR. BARNES: If you recall. You don't have to guess.

A I don't know. I know I have the raw data. I don't know if I saved it in any kind of file.

Q Have you done any of your own analysis of that raw FDA data outside of the context of Q Scan FDA?

A Yes. I was looking at the raw data and comparing it to Q Scan because I was looking for lawyer reports and I wanted to understand what was going on.

Q Did you do that for this particular case?

A No.

Q When did you do that?

A Oh, about a month ago, I believe.

the company gets more information, they can provide follow-ups and they're sequentially numbered.

Q Is there any limit to the number of follow-up reports a manufacturer can send to the FDA?

A Not that I'm aware of.

Q Do you know how Q Scan computes with the last best cases for a particular report?

A We have talked about this. It is supposed to be the most current and most complete case. However, all the information is retained. So if you drill down to the case you'll get all the follow-up reports. So it's all in the database. Nothing goes away.

Q If you were going to look at time trends within the database, it would be important to know the date that a report came in, correct?

MR. BARNES: Objection. You may answer.

A Time trends based on report dates.

Q Based on dates received by the FDA?

A Yes.

Q Do you know how Q Scan deals with the date of a particular adverse event term within a report with respect to multiple versions?

MR. BARNES: Repeat the question for me.

Q Okay. Let me give you a little bit of a

hypothetical.

The initial report comes in on January 1st, 1998 and has the word -- the term headache. You with me so far?

A Sure.

Q On June 1st of 1998, a followup report comes in --

MR. BARNES: 99 or '98?

Q -- 1998, June 1st, five months later, comes in and changes that to migraine, okay. On June 1st of 2004, another followup report comes in which also contains the term migraine. Which date should you assign to the term migraine?

MR. BARNES: Which date should she assign or which date did the Q Scan assign?

Q Which date would you assign?

MR. BARNES: Okay. That's fine.

A Which date would I assign?

Q Yes.

A I don't know. Is it a headache that turned into a migraine? Or was it originally a migraine and it's being recoded.

Q It was not originally -- migraine was not part of the original report. Migraine was not showed up on version 2 of the report?

A I'm not saying migraine is serious or not serious. I'm using the definition of serious from the FDA regulations is based not on the event but on the patient outcome.

Q So migraine could be serious or it might not be serious, it would depend on that particular report, correct?

A It depends on the patient outcome.

Q I don't think we got to where I was -- the answer to my hypothetical. What I really want to know is there were three versions of the report and migraine didn't show up until the second version of the report. Which version of the report should you attribute the date of the migraine --

MR. BARNES: Objection.

Q -- the migraine was first reported?

MR. BARNES: Objection. Asked and answered.

A As I said earlier -- excuse me, as I said earlier it's going to depend on the situation and I can't just guess what the situation is.

Is it correction of a code that was wrong and it was at the same time that they wanted to code migraine and not headache or was it something that developed over time? It was originally a headache and

MR. BARNES: Objection. Assumes insufficient facts to answer a hypothetical.

A I'm not quite sure of the timeline. I understand you said the migraine showed up on the second followup report, but is it a correction or is it a new adverse event and why would migraine even be in there if it's not serious. So I'm not quite sure I understand.

MR. BARNES: That's fine.

MR. ALTMAN: Okay. We need to take a break.

THE WITNESS: Great.

MR. ALTMAN: Change tapes.

THE VIDEOGRAPHER: Going off the record. The time is 10:17 a.m. This is the end of tape number 1.

(Off the record.)

THE VIDEOGRAPHER: We're on the record. The time is 10:31 a.m. This is the beginning of tape number 2.

BY MR. ALTMAN:

Q Dr. Weiss Smith, before the break you had said a statement that migraine, even if it's not serious. Implying that migraine was not serious; is that correct?

now has become a migraine? I don't know with your hypothetical.

Q When you do data mining, which I'm sure we're going to talk some more about, before you do your analyses do you sit and review every single adverse event report up front to see whether it's accurate, to see whether it should have been coded a certain way, to see whether the dates are correct or do you use the database as it exists?

A Data mining, by it's very nature, is mining large quantities of data. And, therefore, you don't go and evaluate all 3 million reports in the AERS database to do data mining. Absolutely not.

Q So if I was going to do data mining off of that database, which version of the report should I attribute the migraine to in terms of its date?

A Again, you don't give me enough information to make sense of that question.

Q It does not show up in version 1, it shows up on version 2 and it also shows up on version 3?

A Again, with your hypothetical I don't know if it's a correction or if it is a newly emerging condition.

Q But from a data mining perspective, you wouldn't have any way to know that and you wouldn't be

looking at it at that level, would you?
A By nature data mining is not looking at the individual cases. It's looking at trends and reporting rates.
Q If I'm looking at the dates attributed to a particular term on a particular report, I have to pick a date. So which date do I pick?
MR. BARNES: Objection. Assumes facts not in evidence. Argumentative. You may answer.
A Well, I don't know what you're doing. So it depends on what you're doing and what the purpose of it is. You might not even use a database at all.
Q If I was interested in knowing how many reports of migraine came in over time to the FDA's database, which date should I use?
A Again, based on what you told me I can't make it -- I can't make a determination.
Q Do you know what date Q Scan does when you did your time trends?
A Time trends?
Q Let's take a step back. In your reports you did some analyses of reports and things over time. Correct?
A That is correct.
Q Do you know for a report that has multiple

versions which date Q Scan uses?
A I would have to go back and check. I believe it's the original date of the report. But I'll have to go and verify that.
Q If it's not the original date, if it's let's say the last date or some date in between, that could have some influence over the time trends, correct?
MR. BARNES: Objection.
A That's making assumption that all reports have follow-ups and the follow-ups are quite different from the original date. So I would have to say no, I don't believe that's usually the case.
There's not that many follow-ups. Every report does not have a follow-up and if they do, they don't necessarily come months and years later. So when I look over a year period, as long as it falls within the same year, they're still going to be the same time period.
Q But you don't know as you sit here what influence that would have over any particular analysis you did, correct?
MR. BARNES: Objection.
A Based on what I know, I would assume that it is little, very small, if any. Particularly when

you look at a year time span.
Q Did you look at that influence for this particular report?
A I did not consider your hypothetical for my analysis.
Q Did you ever work in the pharmaceutical industry?
A I have consulted to the pharmaceutical industry.
Q Did you ever work directly for a pharmaceutical company as an employee?
A As a regular employee, no, as a consultant. But I've worked, for example, for Hoffmann-La Roche. I worked for them as a consultant for three months full time but that's it.
Q When you were consulting for industry, did you ever directly work on a new drug application?
A I've never written a new drug application. I worked on information that might go into a new drug application, yes.
Q You say might go into it. Do you have any specific knowledge of a particular project you may have done for a pharmaceutical company that was used as part of a new drug application or an SMDA or an ANDA?
A I never saw the application so I'd have to

assume and I don't want to do that here.
Q Did anybody ever come to you and say, we would like you to analyze the post-marketing data for a particular new drug application we're going to be doing?
A No. If they asked me to analyze data, that would be just in the general context of doing a study. I don't go and do data analyst -- analyzing for people as a consultant. I look at the big picture and I --
MR. BARNES: Did you finish your answer?
A No, that was it.
I look at the big picture. I don't do ad hoc analysis necessarily.
Q Have you ever been asked to write any portion of an NDA?
A No, I don't do that.
Q Have you ever helped write any report of integrated summary safety?
A No.
Q Have you ever done the analysis of data that goes into an integrated summary safety?
MR. BARNES: At what point in time? Before or after the final NDA? Vague as to time.
Q At any point in time.
A My work is generally for drugs that are

already on the market. My specialty is post-marketing safety and adverse events. So that's the majority of my work is looking at drugs that are on the market particularly for safety concerns and newly evolving signals.

Q I noticed in your report you write some fairly extensive comments on the FDA's -- well, strike that.

The FDA in January, just about three weeks after we took your deposition last time, came out with an alert of antiepileptic drugs and suicidality, correct?

A Yes, they did.

Q And you reviewed that alert, correct?

A I read the alert, yes.

Q And you reviewed the statistical review that the FDA made available dated I believe it's May 23rd, 2008, and made publicly available?

A Yes, I read that version and then I believe they had a later version in June that they gave to the advisory committee.

Q Were you aware that Pfizer submitted an analysis of data to the FDA prior to the advisory committee hearing?

A Which analysis?

Q Are you aware that Pfizer produced any -- provided any analysis to the FDA of the clinical trial data with respect to Neurontin in the records?

A Well, I believe the report from Patel is exactly that. We talked about that at my last deposition. The FDA submitted their data in summary of their data to the FDA which was what went into the FDA analysis.

Q Are you aware of any submission that Pfizer made to the FDA shortly before the advisory committee hearing that took place July 10th of 2008?

A No, not that I can remember.

Q Did you -- so it's safe to say you didn't review that analysis that Pfizer provided to the FDA?

A I'm not sure. I'd have to go and look. I don't know.

Q Did you review the transcript of the FDA -- of the FDA advisory committee hearing?

A Yes, I did.

Q Were you aware that Pfizer made a presentation to the FDA at that hearing?

A Yes.

Q The analysis that I was referring to is the same that Pfizer discussed at that hearing, does that refresh your recollection at all?

A Yes, a little bit.

Q Do you remember reading that now?

MR. BARNES: If you do, you do.

A I'd have to see it, yeah.

Q Were you asked by Pfizer to participate in any documents which they might be submitting to the FDA in preparation of the advisory committee hearing?

A No.

Q Were you at the advisory committee hearing?

A No.

Q Were you asked to be at the advisory committee hearing?

A No.

Q It's relatively close to here, so it wouldn't have been a particularly long trip for you to go to the advisory committee hearing, correct?

MR. BARNES: Objection.

A I'm very busy.

Q But it's not distance-wise very far, correct?

A From my house, it's a couple of hours. So, yes, it's quite a trek.

Q Were you aware that Pfizer made a presentation to the FDA before the advisory committee hearing?

A Not that I recall.

Q Safe to say you didn't participate in the development of any materials for such a meeting, correct?

A No.

Q Okay. Are you qualified to review the FDA's statistical analysis in the advisory committee transcript?

A Excuse me?

Q Do you believe that you are qualified to have reviewed the FDA statistical review in the advisory committee and render opinions?

A Absolutely. That's what I do for the FDA. I often sit on these type of advisory committees. I couldn't sit on this one because I had already been retained on this case.

Q Do you believe that you were qualified to do so in January when we took your deposition last?

A Excuse me?

Q Your qualifications to review this information, is that a new found qualification or is that something that you possessed back in January when we took your deposition last time?

A I believe I was qualified in January to sit on the advisory committee and review the materials.

Yes. I think I've been qualified for years to do so.
Q Were you asked by Pfizer to review those materials within January -- in the January timeframe right after it came out?
A I was provided by --
MR. BARNES: Answer the question.
A By Pfizer? Pfizer didn't -- I didn't directly talk to anyone at Pfizer about this case. Period.
Q Were you asked by counsel to review that FDA and render an opinion?
A They provided me with the alert and the information.
Q Did they ask you to do anything with it?
A Just to reread it.
Q When the statistical review -- when did you first see the FDA statistical review?
A When did I see it? When it was -- after it was made available to the public on their web site.
Q So you didn't see it before then?
A No, I only saw it when it was made available.
Q Do you know if Pfizer had that document before it was made publicly available?
A I'm not aware.

Q Okay. When was the first time you were asked to render any opinions on the advisory committee meeting and the transcript and the discussions that took place?
A I believe it was around the same time.
Q Have you ever had any direct discussions with Dr. Robert Gibbons?
A No.
Q Do you believe that you are -- you're aware that Dr. Gibbons did a pharmacoepidemiologic study of the pharmametrics data, correct?
A Yes, I'm aware of it.
Q If you had been given that raw data as he was, do you believe you could have done a similar study?
A Yes.
Q So you pretty much see yourself as kind of colleagues, same general qualifications?
A I consider us colleagues. He's a biostatistician and I'm an epidemiologist. We typically work together on teams.
Q We talked before about the AIRS G database in this case. Have you ever received similar data from a company in the past? What I mean by that a CD, et cetera, that has their adverse event database or an

Q Were you asked to ever review it at that time?
MR. BARNES: What time?
Q At the time it became publicly available. When we're talking about the FDA statistical review?
A Was I asked to look at it? I think I had already looked at it as soon as it became available because I wanted to put the alert in January in context. So I was very interested in what they said.
Q When was the first time you were asked to put down on a piece of paper an opinion based upon the FDA alert?
MR. BARNES: Objection. We have a stipulation in this case where drafting of expert reports is not the subject of examination. So I'll instruct her not to answer that question.
MR. ALTMAN: I'm not asking about the drafting. I'm asking when she was asked to do it. That's not the drafting.
MR. BARNES: That's a different question.
MR. ALTMAN: I asked when was the first time you were asked to opine upon the FDA alert.
MR. BARNES: That's a different question. You may answer that one.
A I believe it was in early fall.

extract for a particular drug?
A Yes.
Q Did you use that, make use of that data, did you load it into a database? Did you use it in any way yourself or did you do just a quick cursory review of it and put it aside?
A That's a general question for many different situations. So I can't answer just one thing.
Q Have you ever done more with a company's internal adverse event database than you did in this particular case?
A Yes, I have.
Q Did you do that work yourself and did you have people working with you to do that?
A Depends on the situation.
Q Have you ever done it all by yourself?
A Yes.
Q What tools would you typically use to do that?
A Again, it depends on the situation.
Q What tools have you used in the past to do that?
A You mean what software?
Q What software?

A I've used D Base, starting with 2, 3, 4. Okay. I've used Excel. I've used sets, Epicure, Epi-Info. I've used SPSS. Statistical packages, database packages, access. Sometimes I've already been set up in a database. It really depends on what time, the decade, and what I'm doing and how big the database is and where it's located.

Q Is there any technical impediment that would have kept you from doing work with the AIRS G database produced in this particular litigation loaded up into one of those packages and doing computations or analysis or time trending of that data?

A No, it's just a question of time and necessity.

Q Are all reports, strike that.

Does the company have to submit every single adverse event reported received to the FDA?

A It's my understanding that they do not submit every report. There's no need.

Q So there could be and likely would be adverse event data in a company's database that wouldn't be in the FDA's database, correct?

A That is correct. They follow the federal regulations.

Q Do you know what junk science is when I use

statement?

Q That could be.

MR. BARNES: The question is: Have you ever heard junk science specifically as he asked the question? Yes or no? If you haven't, the answer is no.

A I've only seen the term on the internet. I don't use that term, so I'm really not familiar with it.

MR. BARNES: That's responsive.

Q If a scientist comes out with, you know, purportedly research that really isn't, you know -- didn't use sound scientific principles. They just come out with, you know, statements that have no scientific support whatsoever, what do they -- what would you call that?

A I wouldn't call it science necessarily.

Q Well, I'm just looking for a term that we can agree upon to use for that particular kind of practice, your term?

MR. BARNES: If you have one.

A I don't. Depends on the situation.

Q When the FDA makes a statement associated with the approval of a drug that says the drug is safe and effective when used in accordance with the label,

the term junk science?

MR. BARNES: Objection. Vague.

A No.

Q Have you ever heard the term junk science before?

A I've heard it thrown around.

Q Do you have any understanding what junk science means?

MR. BARNES: Objection. In what context?

Q Does it mean anything to you? In any context that you've heard it, do you have any understanding what junk science means?

A It can really mean anything. I mean, what --

MR. BARNES: You've answered the question.

A -- what do you mean?

Q So junk science doesn't have any particular meaning to you? Is junk science sometimes used when people don't follow sound scientific methodologies and just make statements that they can't back up with sound scientific methodology?

A That could be considered junk science.

Q Have you ever heard it used in that particular context?

A Like the earth is flat? That type of

do you rely upon that?

A I'm not a clinician so I don't treat patients so I don't need to rely on it.

Q Do you question, as somebody who interacts with the FDA, do you question whether the FDA was reasonable in making that statement?

A In some circumstances, yes, I do.

Q And I think you have written in the past that you don't always agree with what the FDA has done, correct?

A That is correct.

Q And I think what you just said is you can't always take what the FDA says at face value?

MR. BARNES: Objection. Misstates her prior testimony.

A I think the label is a complicated thing and science is not always so easy to understand. I think you need to understand the context of what the label is and what they're trying to do with the label. And what the label isn't. I think that's very important to put everything into context.

Q What does the term suicidal mean?

A That's been thrown around a lot here. The FDA has used the definition of suicidality based on the Posner classification scheme and there's a number of

terms. I have to go look and make sure I get them all right. There's a number of terms that they included in the report. So within that context we'll go with the FDA's.

Q So if the FDA includes terms like suicidal ideation in the concept of suicidality, you don't have any basis to question that, do you?

A As an epidemiologist we question everything. So, I mean, just put it that way.

Q I'm sorry.

A So within the context of the FDA analysis they define the term suicidality and so I'm going, for that analysis, I'm using the term as they defined it.

Q And that includes suicidal ideation, correct?

A That is what is in there.

Q Do you know what suicide gesture means?

A Yes, I do.

Q Are you an expert in suicidology?

A Absolutely not.

Q What is your understanding what the term suicide gesture means?

A My understanding is it is making some type of action that suggest that there is -- the patient was considering suicide but not something that would have

reached the level of an attempt. So it didn't have potential to be lethal.

Q And what is the basis of your understanding?

A I borrowed a book called Suicide from one of my colleagues to try and understand the whole concept of suicide and suicidality.

Q So I think what you said, if I understand right, is that suicide gesture does not include suicide attempt?

A That is my understanding. It does not reach that level.

Q So --

MR. BARNES: Speaking in terms of -- in what context? In terms of are you talking about coding? Are you talking about generally how the clinician would use it in the textbooks? It's vague.

MR. ALTMAN: I'm asking what she -- she defined what suicide gesture is.

A That's my understanding what it is. Now, I'm not a nosologist. I'm not coding for the FDA. If they have other terms or clinical descriptions, that's not what I'm doing. I'm saying from what I understand.

Q By the way, we talk about FDA coding. Putting electronic submissions to the FDA, which is a

relatively recent occurrence. Let's say within the last three or four years or so, correct, from manufacturers to the FDA?

A I believe there are pilot studies going on a lot longer than that.

Q As a general the prop -- putting electronic submissions away. Do you know if the FDA uses -- strike that.

On a MedWatch form there's a box where the manufacturer can put the adverse event terms that they would like to assign to that particular report, correct?

A This is a place for them to write the terms, yes.

Q Do you know if the FDA uses those terms as selected by the manufacturer?

A It is my understanding that they can use those terms. It's my understanding sometimes they also change or put their own terms in. It's quite variable.

Q Have you ever studied how often the FDA coding is different than that of the manufacturer?

MR. BARNES: At what time period? Today, 10 years ago?

Q Let her answer.

At any time period have you ever studied?

A I do not study coding of the FDA.

Q Well --

A It's a general field of study. Only within context.

Q Well, do you know if it would be difficult if you had a company's internal adverse event database and you had the FDA's database, do you know if it would be difficult to compare the coding between a subset of reports that you could match up?

A It depends on the situation. It could be quite simple and it could be quite difficult.

Q Have you ever done --

A Yes.

Q -- such an analysis?

A Yes, I have.

Q In what context?

A In a different case.

Q Was it for a legal case?

A Yes.

Q Did you find -- we don't have to talk specifically about the case, but did you find that there were differences between the two?

A I did.

Q Do you know about what percentage? Do you have any recollection of how frequently they were

different?
A I was looking at a particular adverse event.
Q So as a general proposition you wouldn't know?
A So for the entire database, no.
Q Okay. If suicide gesture doesn't include suicide attempt, it clearly wouldn't include the term suicide; is that correct?
MR. BARNES: Objection. In terms of clinician, general, coding? You have to have context.
MR. ALTMAN: Her definition.
MR. BARNES: Her definition for what purpose?
MR. ALTMAN: According to her own definition.
Q You defined what suicide gesture meant to you. I'm asking you does suicide gesture include the term suicide?
A If you're talking about a case report, they could have all the terms. I don't understand what you're asking me.
Q Does suicide gesture -- you said it doesn't include a suicide attempt, is not a suicide gesture. Is completed suicide suicide gesture?

MR. BARNES: Objection. Again, clinically, labeling, coding? It depends on the context.
MR. ALTMAN: Rick, it's her own definition. She defined that suicide gesture did not include up to the suicide attempt. Then I asked her did suicide attempt include a suicide gesture. She said no.
Now I'm asking if completed suicide --
THE WITNESS: I didn't --
MR. BARNES: I don't think she stated --
THE WITNESS: I don't think so.
MR. BARNES: You may answer.
BY MR. ALTMAN:
Q Let's go back. You said suicide gesture is up to suicide attempt; correct?
A No, I don't believe I said it like that.
Q Let's check what you did say so we're sure. I want to get it right.
You said my understanding is it is making some type of action that suggest that there is, the patient was considering suicide but not something that would have reached the level of an attempt so it didn't have the potential to be lethal?
A Right. It didn't have the potential to be lethal. That's what I understand suicide gesture to mean.

Q Then I asked you, you can only tell me what your understanding is, I asked you it does not include suicide attempt. You said, that is my understanding it does not reach that level.
A That's my understanding that a suicide gesture is not identical to a suicide attempt. Otherwise they would just call it the same thing.
Q Now I'm asking, does it also mean a completed suicide? Just like in the same context of suicide attempt?
A I believe that completed suicide has a different definition than suicide gesture.
Q So does everybody who has a suicide gesture complete suicide?
MR. BARNES: Say that again?
Q Does everybody who simply has a suicide gesture, as an adverse event, do they also all complete suicide?
A I believe many people who have -- from my understanding the numbers -- I don't know particularly for suicide gesture but I know for suicide attempt there's many more attempts than there are completed suicides. So I would have to assume that the same situation is true for suicide gestures. But that's an assumption.

Q Would the term completed suicide be more specific if we were talking about suicidality and suicide issues? Is the term completed suicide more specific than suicide gesture?
A From the terms of accurately measuring, from an epidemiologic standpoint, yes, I believe it would be a more concrete term.
Q Okay. Do you have any opinion as to whether a doctor is qualified to determine that a particular drug is working for that particular patient? When I mean working, providing the benefit that they expect it to have?
A That's really too broad to answer.
MR. BARNES: Actually that's no.
A No.
Q So --
A Not in that context.
Q If a doctor prescribes a drug to his patient, is he qualified to tell whether the drug is helping that patient?
A Maybe.
Q When would he be qualified and when wouldn't he?
MR. BARNES: Objection. Calls for speculation. If you know. If you're qualified to

assess that.
A One, I can't make the assumption that every doctor is qualified to practice. One. Two, I can't make the assumption that every doctor monitors and can tell whether a drug is working or not. Some it's very easy to tell and some it's much more difficult.
Q So what I think you're saying is sometimes a doctor can tell that the drug is actually working for their patient?
A Sometimes. Depending on the drug it's very obvious and sometimes it's not very obvious.
Q Can sometimes a doctor tell that the drug is harming their patient?
A Sometimes it's obvious and sometimes it's not so obvious.
Q Are you aware of whether there are any drugs that have been approved for indications which the efficacy was demonstrated by subjective patient statements?
A Could you explain what you mean by that?
Q Sure. Take depression. Is there a scientific method that you can objectively determine how depressed somebody is?
A There's are a number of scales that are used.

Q Are they objective in that you can hook up a machine to somebody and you can tell how depressed they are, or does it require some kind of subjective input from the patient to provide the data for the scale?
A My understanding that it requires some input from the patient.
Q Do you know of any studies out there that can measure somebody's depression without subjective input from the patient?
A Not that I'm aware of.
Q And there are drugs that are approved for the treatment of depression, correct?
A Yes, there are.
Q And so they're approved based on subjective input from the patient, correct?
MR. BARNES: Objection. If you know.
A Not in the context you're using the word subjective.
Q Okay. The very lowest level of whether the drug is working is a subjective statement from the patient, correct?
A No.
Q How --
A When you're talking about scales, it's not

just hey, is a drug working or not. They're validated, they're tested. There's not just one question. There's a series of questions. There's a series of measurements. They're objectively defined. They're set up in advance.
So it's a very stringent criteria using a scale that's validated. So it's not just have a mere subjective outcome.
Q But the source data to feed into the instruments is subjective data from the patient, correct?
A I can't say it's all subjective. There can be some objective. Some very concrete yes, no, did this occur.
Q Okay.
A So I don't want to have a blanket statement.
Q Does subjective information form part of the basis of those instruments, of the data for those instruments?
A The patient's self-assessment of their feelings?
Q Yes.
A That's what I understand it's part of the overall measure.

Q Okay. So drugs for depression are approved in part based upon, at its very lowest level, patient's self-assessments of how they're feeling, correct?
A That is a very broad statement. So in its totality it's not correct.
Q The instruments that are used to measure efficacy rely upon patient's self-assessments?
A In part. Same with pain. We ask people on an objective scale to rate their pain. So there are definitely measures where you ask a patient to objectively rate what's going on. But they're collected in such a way that they -- it's not just a subjective -- I feel better type measure. There's definitely different components of depression that are measured and put together into a scale.
Q But in part those rely upon subjective self-assessments, depression, pain, any of those things, correct?
A In part they rely on the patient's self-assessment.
Q So, in part, the demonstration of efficacy of a particular antidepressant drug is based in part upon patient's self-assessments?
MR. BARNES: Objection. Asked and answered. You may answer again.

A I said part of the scale may be a patient assessment. Yes.
Q Can a patient's self-assessment reporting harm also be part of the basis of concluding that a drug causes harm?
A Without any context I can't answer that.
Q How do you demonstrate efficacy for a drug?
A Based on the federal register there's a standard of well-controlled studies to present efficacy. So there's standards and regulations and guidance with the FDA to show what needs to be done to show efficacy.
Q Companies, besides randomized well-controlled trials, also do open label studies, correct?
A That's my understanding.
Q And it's part of the basis that they use to support their new drug applications, correct?
A It's not part of the basis for efficacy.
Q But do you know why companies do open label studies?
A I think it varies by drug.
Q Do they submit these open label studies as part of their new drug application?
A My understanding the FDA requires them to

submit all experiences from -- in clinical experiences as part of the application.
Q And open label studies are typically not controlled in the context of an epidemiologic study, correct?
A It depends again within the study and what's being done. So they can be controlled or they can be uncontrolled.
Q Are they done with any less scientific rigor than a randomized controlled trial?
A Again, I think it would depend on the context of the trial.
Q Do you understand what I mean by rigor? I mean, do they carefully track their patients in inclusion and exclusion criteria?
A Again, I don't want to make a blanket statement. I assume in some cases, yes, and probably in some cases not as rigorous as a clinical trial. So again it would be very situational dependent.
Q Did you review the new drug application for Neurontin? The original new drug application from 1994?
A I know I saw some things, but I don't know if -- I don't believe I saw the entire dossier. I can look. I did see Dr. McCormick's review and evaluation

of the safety update in 1993.
Q I'll ask a different question. Why don't we -- strike that.
It appears from your first list of materials considered you looked at about four or five Pfizer research reports. Does that sound about right?
MR. BARNES: Can you refer to what you're looking at?
Q If you take a look at your first -- I believe it's Exhibit 21. On page one I see towards the middle column, do you see RR reg 7230135PH and integrated summary?
A Yes.
Q Then I see numerous papers listed and then it looks like on about page eight you list three more research reports?
A Okay.
Q And I don't see any in your new reports. So it looks like you reviewed about three or four research reports in this case. Does that appear to be correct?
A That appears to be correct.
Q Do you have any understanding of how many research reports Pfizer has on Neurontin?
A No, I'm not aware.

Q Did you review, aside from the bi-polar studies, the psychiatric studies listed on page eight which I believe were -- it says bi-polar panic disorder and social phobia. Did you review any other individual research reports for individual trials?
A Everything I reviewed is on one of the two lists. So nothing that is not listed.
Q Are you aware of whether depression has any kind of periodic nature to its severity for a given patient, all things being equal?
A Not being a clinician, I don't want to speak as a clinician, but as a lay person and from the research that I've done, yes, I'm aware that depression can be episodic.
Q Is that the same thing with pain?
A Some people have chronic pain. Some people have acute pain. It can be episodic. Again, it varies.
Q In a clinical trial that's based on subjective feelings, it's possible that somebody comes in and is feeling better that day because it's episodic, you know, the episodic nature of their disease and has nothing to do with the drug that particular day, correct?
MR. BARNES: Objection. You may answer if

you know.

A Again, we talked about the fact that it is not purely subjective. So I don't want to be boxed in saying that it's only subjective.

Two, that's why they have controlled clinical trials. There's something called the placebo effect. Also people can just feel better, yes, and it can be episodic.

Q Okay. Now, there's obviously some terminology issues in the use of the term signal in a pharmacoepidemiologic concept. So I think we should clarify so we can talk the same language for the rest of the deposition because you use the term signal and there's also the term signal of disproportional reporting, we'll call it SDR. I think that's your definition or that's conventionally used.

Is there a difference between signal and SDR?

A Yes. And actually it's not my term. I spent a few days with Ralph Edwards two weeks ago and he told me that that SDR is Manfred Hauben's term which he objects to and that he only likes disproportional reporting.

Alert and signal of disproportional reporting or disproportional reporting, depending on

which side of the ocean you're at, all of those terms are synonymous. Signal is not synonymous.

Q Okay. The terms that refer to disproportional reporting, what does that mean?

A I'm using them within the context of data mining.

Q Okay.

A The term alert or signal of disproportional reporting or disproportional reporting is purely statistical that you established a threshold and defined a test statistic based on whatever algorithm you're choosing to use and you've defined that as what is statistically elevated.

So an alert would be any time you have a term that is seen, disproportionally reported, above that threshold, whatever it would be, that would be called an alert. It's purely statistical.

That differs from what we would call a signal, which is once you take those and you triage them and you evaluate them within the clinical context, again, this is usually the clinical evaluation of the statistical alerts. If there's something that is clinically relevant or meaningful, that becomes then a signal. At that point one could form a hypothesis and follow the signal up by doing a study to see if there

is indeed a statistical association.

Q Which term would you prefer to use for the purpose of this deposition referring to disproportionality?

A Why don't we stick with alert and keep it simple.

Q That's fine. We'll use the term alert.

If you detect, you said something about algorithm. We'll talk about them later. It doesn't really matter.

You see an alert, is it appropriate to simply do nothing about that alert?

A In what --

Q To just simply say, ahh, this appears to be an alert, it meets my threshold, I'm going to ignore it. Is that appropriate?

A In what context?

Q In the context of data mining?

A In what context?

Q I've done some kind of data mining and I see an alert, for whatever the threshold that particular person defined in that particular methodology, I see an alert, is it appropriate to simply ignore it?

A It depends on the context. I do data

mining all the time. I don't act on every single thing that goes above the threshold. Do you?

MR. BARNES: You don't ask.

A Sorry.

MR. BARNES: You answered the question.

Q When you choose not to do something, though, are you using some other knowledge that you have that that alert may be spurious, may be unimportant, not clinically meaningful? You put some context around that alert before you decide not to follow it up, correct?

A Again, it depends on the context of which one is working.

Q All right. We'll come back to this.

We have talked about pharmacovigilance and pharmacoepidemiological. Are the two terms synonymous?

A Some people think they are. I tend to consider them complementary but not synonymous.

Q So is it a reasonable statement to say that one of the tools of conducting pharmacovigilance is pharmacoepidemiology?

A I believe so. And vice versa.

Q Pharmacoepidemiology is a relatively new field, isn't it?

A Well, as I get older, it gets older. So I

think it's been around for a couple of decades now.
Q And data mining is a relatively new process?
A For pharmacovigilance it's only being adopted now and it's a recent development. But it's been used in other fields for many years.
Q In conducting pharmacovigilance we have said one of the tools is pharmacoepidemiology. Is reviewing individual case reports part of pharmacovigilance?
A That is a classic part of pharmacovigilance, yes, to do individual case report reviews.
Q Do you always, as part of pharmacovigilance, do you always do a pharmacoepidemiologic study when you see a possible signal?
MR. BARNES: Objection.
A Do I personally?
Q Do you personally?
A If I don't have funding to do a study, I don't do it. I don't always have the staffing to do that.
Q You've talked with a lot of people in the industry about how to conduct pharmacovigilance and

company go out and do a pharmacoepidemiological study every time they see an alert?
MR. BARNES: To your knowledge. If you know.
A I don't know the SOPs for every company. I don't even think every company data mines from what I understand.
Q I wasn't talking about data mining. I was talking about pharmacoepidemiologic study?
A You said alert.
Q From an alert?
A That's assuming people data mine because we said in the context we would use alert to be a signal of disproportional reporting.
Q You're right. All right. That's fine.
Are there things other than alerts that could trigger your need to do a pharmacoepidemiologic study in the absence of data mining?
A That's my understanding.
Q Could a series of cases of a particular adverse event trigger that you need to look at it further?
A Who is you?
Q A pharmaceutical company?
A Potentially.

pharmacoepidemiology, correct?
A Yes. We have had a conference most recent.
Q And, in fact, I think you did a pretty extensive study on how companies are using pharmacoepidemiology and data mining and things like that, correct?
A It wasn't that inclusive, no.
Q But it was a study of trends and what people are doing these days, correct?
A It was specifically looking at data mining. Not the whole pharmacovigilance process.
Q Before data mining people still conducted pharmacovigilance, correct?
A That is correct. It is only a tool.
Q And people do pharmacovigilance in the absence of pharmacoepidemiologic studies, correct?
A I don't believe so.
Q Does every time somebody sees an alert, do they go out and do a pharmacoepidemiologic study? Sees a signal -- sees an alert?
MR. BARNES: Objection. Vague as to who somebody is, what the context is. Overbroad. If you understand that question, you may answer.
A I don't understand it.
Q I'll ask a different question. Does a

Q Is it possible that a single adverse event report could trigger that the company might need to investigate to understand that adverse event better?
A It would be unusual. But anything is possible in that context.
Q Has that happened?
A Not that I know of personally. I can't say this case triggered a pharmacoepic study, no.
Q Do you always have to do a pharmacoepi study before you take -- make labeling decisions?
A Not necessarily.
Q So we're getting back and talking about alerts. What do you think is the appropriate response to an alert? I've seen an alert. What do I do next?
MR. BARNES: Objection. Overbroad. Lack of foundation. Go ahead.
A Are you talking about the company perspective? FDA perspective?
Q From a company perspective.
A I think all companies, before they institute data mining, should develop SOPs on how they're going to triage signals of disproportional reporting.
Q In your experience what do you recommend a company does in response to an alert?

MR. BARNES: At what period of time, today?
Q Today.
A I recommend that every company establish standard operating procedures on how they're going to deal with it.
I think it very much depends on the company, on the drug, on what they're data mining in, what the purpose is. So they really need to set up a system.
Uppsala has a wonderful triage system that they actually publish and one can look at as an idea. But again the company has a different perspective than a regulatory agency. So it's going to depend on who you are, what your drugs are, what you're doing.
Q Before data mining, I don't want to use the term alert, but there could be other information that could kind of take you to the same place as you would have been if you had gotten an alert through data mining, what can we call that?
A Are you talking about alert or a signal?
Q I see something through -- I'm not doing data mining. I see something either through a few case reports or something like that that causes me concern that I want to follow-up.
So it's, you know, it's not an alert

because we have agreed that that only comes from data mining. But what do you call that in the old way before you had data mining? What can we call that?
A I thought we were calling that a signal. Because that has some clinical relevance.
Q So if there is --
A Why else would you want --
MR. BARNES: You answered the question.
A Okay, sorry.
Q So just to make sure that I understand. If I'm not using data mining, I can kind of shortcut the process if I see a number of case reports that cause me concern, is that a signal?
MR. BARNES: Objection. Overbroad. Vague.
A Why -- it depends on why it's causing you concern.
Q I don't expect -- through my routine post-marketing safety surveillance a number of reports come in for a particular adverse event I don't expect to see. Okay. I think that that needs to be followed-up. Is that a signal?
A It depends on why it is of concern.
Q I've decided -- if -- I'm in post-marketing advance. I decided I need to evaluate it. I've already made that decision. Do I have a signal?

MR. BARNES: Objection. Overbroad. Vague.
A Again, it depends on the context of why one has decided that it's important to go to the next step.
Q Okay. Are there circumstances where I would go to the next step that it would not be a signal?
A I don't know. That's a good question.
MR. BARNES: You answered.
A I mean, hypothetically who knows why someone, you know, would have a reason to go if there's something that's not clinically relevant.
It's very expensive to do an epidemiologic study but you never know. There might be something that's so important that somebody wants to follow it up even if they don't see something. I can't imagine, but it could be.
Q What is the difference between -- strike that.
So to make sure that I understand. Our two paths to signal are through some kind of alert, which I do some follow-up on. Maybe I find some case reports. I do some literature research, whatever, and I decide that it's a signal. Or, I kind of don't deal with the alert process and the data mining there's something catches my eye. Clinically, I'm a, you know, I'm a

doctor and I'm a clinician within the pharmaceutical company and reviewing spontaneous reports and I see something that catches my eye and I do some further research and some follow-up through the literature.
I can get to the same place through either path, correct?
MR. BARNES: Objection. Overbroad. Vague.
A As we said signal is something that has clinical relevance. So if it has clinical relevance that might be one of the criteria to follow-up. Potentially.
Q Were you done?
A Yes.
Q What is the difference between a signal and an association?
A Within pharmacovigilance we use the term signal for data mining is the -- an alert, disproportional reporting plus some clinical relevance. That's it.
If you do an epidemiologic study you might look and do an analysis to see is there a statistical association between an exposure and an outcome. So that's based on a research study.
Q Do you have to have a statistical association in order to take regulatory action in terms

of changing the label?
MR. BARNES: If you know.
A It is my understanding that FDA does not always have epidemiologic data and can act on changing a label within any context.
Q You say FDA can act, but a company also could act on changing a label, correct?
MR. BARNES: Objection. If you know.
A I'm not as familiar with the thresholds of the company needs to change their label. But it -- it always -- they always have to work with FDA to do so.
MR. ALTMAN: I think we need to change tapes.
THE VIDEOGRAPHER: Going off the record. The time is 11:29 a.m. This is the end of tape number 2.
(Off the record.)
THE VIDEOGRAPHER: We are on the record. The time is 11:49 a.m. This is the beginning of tape number 3.
BY MR. ALTMAN:
Q Before data mining and in the absence of data mining even today, what are the general steps a company should be implementing in terms of post-marketing monitoring for the safety of their

drugs?
MR. BARNES: Objection. Vague as to time. Are you talking about today or 1999, 2005? I mean, there's -- it may change over time. There's not -- you should put it in context.
Q In the absence of data mining, has pharmacovigilance changed over the last 10 years shall we say?
A I can't really say. The clinical pharmacovigilance function outside of data mining is not my expertise. I'm not testifying on that.
Q So let me ask you a question: Have you ever, putting any data mining aside, have you, yourself, ever determined that there was a signal that needed to be followed-up in the context of post-marketing safety surveillance?
A That's a clinical decision. So no, that is not what I do.
Q Have you ever taken an alert and done the research that goes along with finding the clinical information or the other stuff to put the alert into context to conclude that there was a signal?
A At this point, no. I look at the data mining alerts. I've had a study where I've had a clinical staff go through and look at the clinical

relevance and then we have matched them up and down a validation study, in that context only, with a full team of experts.
Q Have you ever designed a post market -- have you ever designed post-marketing safety surveillance for any pharmaceutical company?
A No, I've not developed pharmaceutical SOPs. I've developed guidance from industry from the FDA perspective, I've worked on those. But not within companies.
Q Which guidance did you work on that would be relevant to pharmacovigilance and safety surveillance?
A I've worked on -- actually, I was the co-author of the original draft of the pregnancy registry guidance document. I started that while I was at the FDA and then they paid me as a consultant afterwards.
I also worked at the very beginning on the original concept and drafts of the good pharmacovigilance -- what became the good pharmacovigilance and pharmacoepi guidance document.
Q That's the guidance from 2005?
A Right. I worked way early on the very, very beginning of that document.

Q When was that?
A When I was at the FDA in the late '90s. It was much smaller then. It kind of took on a life of its own.
Q Yeah, I'm quite sure. Regulatory agency calls a pharmaceutical company and says, hey, we need to evaluate a particular safety issue. Is that a signal?
MR. BARNES: Excuse me. Objection. Please repeat. That I didn't hear.
Q I said, if a regulatory agency called a pharmaceutical company and says, we would like you to evaluate a particular safety issue, does that constitute a signal?
MR. BARNES: Objection. If you know.
A From my perspective? That's not how -- what I use as a signal, no. From my perspective it is not a signal.
Q I think you said before -- this is where I get confused -- we talked about evaluating something seen clinically means that you have a signal and I don't think you could give me an instance where it would not be a signal. I think I asked you that?
MR. BARNES: Objection. Misstates prior testimony. Go ahead.

A You didn't tell me anything in your question about clinical relevance. You just said the FDA tells a company to do something. I don't know in what context the FDA would tell the company to do something. I could be many, many reasons. I don't want to speculate on that.

Q What reasons would you think the FDA would call a company and ask them to evaluate the safety of a particular issue with a particular drug?

A There could be many situations, many reasons.

Q Okay. Can you give me some that you can think of?

MR. BARNES: Objection. Calls for speculation.

A I mean, it's huge.

MR. BARNES: Go ahead.

A I mean, it's huge.

Q Can you give me one?

A One. The FDA reviews a new drug application for a different drug in the class and finds something in the clinical trial, they might want to know if the other companies had seen that in previous work. So they might ask the companies to follow-up.

Q Would you consider that to be a signal?

A For which drug?

Q For the -- not the NDA they're approving, for the company that called asking them to research the issue?

A Not in the context that we're using the term signal, no.

Q What would you call it?

A That the company asked them to follow-up on something.

Q Okay. If the FDA has a safety concern and calls the company and specifically asked them to review a particular issue, does that constitute a signal?

MR. BARNES: Objection. Asked and answered. Go ahead.

A We use the definition of signal here which was data mining which was there was a statistical finding of disproportional reporting for a drug and event pair and then that was reviewed and there was found to have some clinical meaning or relevance and those two combined became a signal. But we're speaking of a specific drug. You're just talking in generalities.

Q There's no data mining. You said you could also get to the same point without data mining through a clinical review of information. You could see

something clinically that causes you a concern that you choose to follow-up to see if there's some relevance to it, correct?

MR. BARNES: Objection. Misstates her prior testimony.

A Companies are required to have in place standard operating procedures to review the data that comes in. So they should follow their SOPs and follow those.

So I talked about signals just in the context of data mining with the alert and then clinical relevance to differentiate between an alert and a signal.

Q Well, we talked a bit before that you could get to the same place, you could get to a signal without data mining, correct?

A Not in the way I'm using the term signal in this context.

Q Before there was data mining people still found signals, correct?

A People reviewed adverse event data, is that what you're talking about?

Q People reviewed information and found signals even before we had data mining or today even if they don't use data mining, correct?

A That's using the term signal in a different context from the way I've been using it in this report.

MR. BARNES: So you --

MR. ALTMAN: Hold on.

Q We talked about alert as an SDR and then you said alert plus clinical information equals -- potentially equals a signal, correct?

A Alert with clinical relevance would then go --

Q Reviewing case reports, doing literature searches, other analyses and things like that, correct?

MR. BARNES: Objection. Misstates her prior testimony.

Q Okay.

MR. BARNES: I mean, I think you're trying to -- you're talking either past each other or she's defined the signal very precisely how she uses it in this case and this report. You keep trying to have -- ask her --

MR. ALTMAN: We're missing each other. I'm utterly confused as we're using the term. And it's very important.

MR. BARNES: She stated it several times what she considers to be a signal in the context of this case and her work, which was the alert plus

clinical relevance, right?
THE WITNESS: Right.
MR. BARNES: The alert being on disproportionality basis, right?
MR. ALTMAN: Rick, I understand that. That's not my concern right now.
BY MR. ALTMAN:
Q I'm asking about can you get to signals in the absence of data mining. I believe I asked that already.
A That's a whole different process that I'm not -- I haven't reviewed anyone's work in it. I don't want to make a judgment about it because that's really outside the realm of what I do.
That's a clinical issue and that's -- I don't want to even guess on how a clinician forms a decision that something is a signal and is not a signal. It's beyond what I do.
Q I'm not asking you to do that.
A Right.
Q What I'm saying is that you can get -- you can find signals without data mining, correct?
A I don't want to say what it is that does and does not make a signal.
Q I'm not asking you what it is. I said as a

general proposition have people in the past, in other context, found signals of potential problems in a drug that they didn't know about without using data mining?
A I defined signal here in this context within data mining. So I --
MR. BARNES: You'll have to explain what you think about a signal.
A Right. What are you --
MR. BARNES: She's using signal very specifically as to the context of the alert process. There's a disproportional reporting or some sort of signal of disproportionality and then having reviewed in the context of clinical relevance. That's what a signal is.
Now if you want to have -- you can't get to a signal unless you do those two steps. Now, you're talking about another type of signal.
MR. ALTMAN: Rick, Rick --
MR. BARNES: That's why you're talking past each other.
BY MR. ALTMAN:
Q You've been working with pharmacoepidemiologic and pharmacovigilance for many years, correct?
A That is correct.

Q You were doing that before there was data mining, correct?
A Yes.
Q People did pharmacovigilance before data mining?
A But I didn't do pharmacovigilance. I did pharmacoepidemiology.
Q So one of the things I want to understand with the -- in your report, you are not expressing any opinions on any of the pharmacovigilance activities that the company did or didn't do outside of the context of data mining; is that correct?
MR. BARNES: Objection.
A I go beyond data mining because I also look at the clinical trials, the database into the FDA, the FDA reports, so I look at the epidemiology in the literature. So I have looked well beyond just data mining.
Q But you didn't look at all the clinical trial reports, correct?
A I looked at the summaries of all the clinical trials; the analysis that was based on the trials.
Q When you say the analysis, are you referring to the company's response to the FDA in terms

of the FDA's inquiries in the 2004, 2005 timeframe?
MR. BARNES: 2006 timeframe.
Q 2004 to 2006, I'm sorry.
A Yes. As specified in my materials reviewed.
Q Did you review any company SOPs for pharmacovigilance at all?
A No, I did not.
Q Do you have any knowledge as to what -- you're aware that before Pfizer purchased Parke-Davis Warner-Lambert back in, I think, about 2000 or 2001, correct?
A I was made aware of it as I was reviewing the documents.
Q Okay. Do you have any knowledge as to what Parke-Davis, Warner-Lambert did in terms of pharmacovigilance in the period before Pfizer purchased them?
A No, I do not.
Q So your opinions do not affect anything that Parke-Davis Warner-Lambert did, correct?
A My opinions are purely based on the -- for the alert is -- is there or is there not a statistical alert. I'm not talking about what their process is for pharmacovigilance.

Q That's why I want to be very precise and where there's a difficulty in the word signal. When you say, as you do many times in your report, there was no signal, you are making that in the context of a signal that would be dependent upon some kind of a data mining alert, correct?

A I'll have to go through my report and see where I use the term signal. Can you --

Q We're going to -- just as a general proposition. You're not referring to whether in the absence of data mining whether some clinician should have seen that there was some potential problem that was uncharacterized in Neurontin, correct?

A I'm not making any clinical judgments because I'm not a clinician.

Q Okay. So I just want -- I want to be very precise about as you use the term signal. So you are only -- whenever you use the word signal in your report you are talking about what you have defined as a alert plus clinical significance, correct?

MR. BARNES: Before you answer that you better read your report.

A I need to go and make sure.

MR. BARNES: Make sure.

Q Well, you can do that during lunch. I

back. She may have referred to Dr. Blume's discussion of the signal. She would be using the context of that.

There's any number of context in which the word signal could appear in her report. You've asked her a very broad question. She's had two reports in this case. If you want her to actually answer the question, she needs to see how it was used. That's what's fair. You've withdrawn the question.

MR. ALTMAN: I'll withdraw the question, that's fine.

Q But as you sit here today, I think you've told me, you are not qualified to determine whether there was a signal absence of data mining or anything like that from a clinical perspective, correct?

MR. BARNES: Objection. Misstates her prior testimony. State your qualifications, as best what your qualifications are.

A I'm an epidemiologist. I do work in pharmacoepidemiology. So that includes research on identifying new signals, following up on potential problems. Also risk management of known problems.

What I did in this case is review the epidemiologic literature, reviewed the FDA analysis and I did some independent data mining of the FDA FOI database. So all of my opinions are based on that

don't want to spend a lot of time doing it right now.

MR. BARNES: We can come back. Well, she's submitted several pages of a report. If you want to ask that question about specifically, she needs --

MR. ALTMAN: I'll withdraw the question. I'll ask the question differently.

MR. BARNES: Okay.

Q Just to make sure and we can put it to bed.

You use the term signal to only mean data mining -- alert plus clinical significance, correct?

A That is how we just defined it for the purposes of our discussion here today, yes.

Q And that's the context in which your opinions are, we're talking about Neurontin, we're talking about your opinions related to Neurontin, that is the context in which you're using the word signal within this case, correct?

A Within this conversation. I need to go back and review if you want to -- me to answer that past question. I want to make sure --

Q Frankly, I don't know how you're going to review 50 pages of report.

MR. BARNES: Well, in order to answer your question accurately she will need to review her report. You asked her about the report. She'll have to go

work.

Q That's fine. Does a company have to prove a causal relationship to change a label?

MR. BARNES: Objection. If you know. Does a company have to prove a causal relationship? Objection. Vague.

MR. ALTMAN: It's not a vague question and she's put herself forth as a regulatory expert.

MR. BARNES: You may answer the question if you understand the question.

A Could you repeat that?

Q Does a company have to prove a causal relationship to change a label?

A To change a label? It is my understanding that there are many things on the label not all of which are definitively proven from scientific research to be causally related. As for changing the label, I have no opinion on that. I have to review the regulations.

Q I believe, I don't have it here, we can check it, that the FDA's statistical review they concluded the relative risks for Neurontin and suicidality was 1.57 with a confidence of interval of .12 to 47.66. Does that sound -- comport with your memory -- and it's not -- the precise numbers are not

important to you.
MR. BARNES: I think --
A I'd like to see the report if we're going to talk about the report.
Q This is the only question I'm going to ask about it so I don't think you need to -- I'll ask the question differently.
You have a relative risk of 1.5 with a confidence interval of 0.1 to 10?
MR. BARNES: Zero point to 10.
Q Does that allow you to conclude that the relative risk is not 0.2?
MR. BARNES: Objection. Vague.
A In what context.
Q Does that -- what does the confidence interval mean?
A A confidence interval, with -- depending on the width of the confidence interval, what limits you've set it at, it would tell you within that specified probability the likelihood that you would have a result that falls within that.
So it's if 95, 95 percent confidence, if you repeated the study 100 times, the results would fall within those limits. So based on statistical theory.

Q So given a 1.5 with a confidence interval of 0.1 to 10, does that allow one to conclude that the relative risk is not 0.2?
A Your question just doesn't make any sense.
MR. BARNES: Why don't you repeat the question.
Q I'll ask it differently. We'll come back to it a different way.
I'm not asking what is the most likely value. Strike that.
A Aren't you, though?
MR. BARNES: Don't --
Q That's not what I'm asking. Strike that.
Confidence interval -- the relative risk of 1.57 with a confidence interval of 0.1 to 10 says that you would expect that your true relative risk lies, assuming it's at the 95 percent level, gives you some comfort saying your true relative risk probably lies between 0.1 and 10, correct?
A Not clear from what you're asking me if I can answer that.
Q Okay. What does 1.5, a relative risk of 1.5 with a confidence interval of 0.1 to 10 mean at a 95 percent level?
A 95 percent level, okay. 1.57 would be your

point estimate.
Q Okay.
A But I'm not clear what -- your point estimate you're referring to. It depends within the internal and external validity of the study. So you have to put things into perspective what kind of study and what you've done.
Q Putting all of that aside. I'm talking about the interpretation of this particular number, if that's a relative risk. All I'm trying to understand is that does that confidence interval allow you to exclude any number between the confidence interval and say it can't be that number?
A It is all based on probabilities and it doesn't mean that they're all equally likely.
Q I understand that. I'm just --
MR. BARNES: Did you finish your answer?
A Sure.
MR. BARNES: Next question, please.
Q You say they're not all equally likely, but does it allow you to exclude any value between those confidence intervals and saying it can't possibly be this, the probability is zero that it is this?
A It's only saying that there's 95 percent likelihood that it would fall within the range. So you

still have likelihood that it could fall outside that range, too.
Q That's not what I'm asking. Does it allow you to say that any value between that confidence interval has a probability of zero for being the true relative risk?
A You're 95 percent confidence -- within the 95 percent confidence interval so the probability would not be zero for any one data point within there.
Q So 1.5 with confidence interval of .1 to 10, the true relative risk could be .2 or it could be .8 or it could be 1 or it could be 5 or it could be 9, correct?
A It could be any number within the confidence interval or outside of the confidence interval.
Q So you can't say that the absence -- the fact that 1 is included in that number there means it cannot be greater than 1, correct?
MR. BARNES: Objection. Vague. Can you repeat the question?
Q I'll it ask a little different. 1 is included in a confidence of .1 to 10?
A That is correct. Number 1 is included.
Q Does that -- can you say definitively given

that relative risk and that confidence interval that the relative risk is less than 1?

A In the context of an epidemiologic study with such a broad confidence interval and such a small relative risk, you're very hard pressed to say that there's any effect at all. But that's how I'm interpreting it as an epidemiologist.

MR. ALTMAN: Objection, nonresponsive.

Q Can you say that it cannot be less than 1?

A As I said it could be any number at all, the confidence tells you the likelihood of certain numbers.

MR. ALTMAN: Objection. Nonresponsive.

MR. BARNES: You're saying that the point estimate is 1.5 but it encompasses a relative risk of 1, correct, and it goes up --

Q It's .1 to 10. All I'm simply asking is can you say that the probability that it is less than 1 is zero.

A If you're stating the confidence intervals you cannot say that there's no possibility that it doesn't fall anywhere in those confidence intervals.

MR. ALTMAN: Objection. Nonresponsive.

Q It's just can you say that the probability it is less than one is zero?

statistical theory, I can't say what the truth would be. It depends on the study and the context of the study and how well it was done and confounding and bias. So you have to put all of that into consideration.

Q But the interpretation of just this number, can you say that the relative risk cannot be less than 1?

MR. BARNES: Objection. Vague. If you can answer that question. If you can't tell him you can't answer it, tell him why.

Q It's not really a trick question.

A I just don't understand what you're -- what you're asking me. I thought I answered it.

MR. BARNES: Let him ask it again.

Q Can you -- with a relative risk of 1.5 and a confidence interval of 0.1 to 10, can you say that the probability that the relative risk is less than one is zero?

MR. BARNES: You have to -- if you can answer that question as stated, tell him. If you can't, tell him you can't answer it.

A There's -- I would have to look and do some calculations. I can't tell you what the probability of any one number is. It's just statistical theory.

MR. BARNES: All you can say is it's statistically significant.

Q It's a yes or no question. Can you say that the probability less than one is zero?

A Probability that it's less than one that's it's protective --

Q Is zero. That there's no chance that it is protective?

A Based on the study, if you believe --

Q Forgetting about that. You believe the numbers. Can you say it is not protective?

A With those confidence intervals you cannot say much of anything.

Q Can you say it is not protective?

A I mean that's -- can you say it is not protective?

Q Can you say that the relative risk cannot be less than one?

A The relative risk is 1.5.

Q Can you say that -- but that's your point estimate, right?

A Right.

Q And you expect your true relative risk to be somewhere in that confidence interval, correct?

A If I repeated the study, based on

Q I'm not asking what the probability is. I'm asking is it zero. Is it impossible that it's less than one?

A It's not impossible.

Q Is it impossible it is greater than one?

A It is not impossible.

Q So in other words that confidence interval does not allow you to draw a conclusion one way or the other as to whether there was a protectful or harmful effect, correct?

A The confidence interval tells us what is the 95 percent probability of range if you repeated the study. That's all it does.

MR. ALTMAN: Objection. Nonresponsive.

Q That confidence interval does not allow you to make a conclusion one way or the other whether it is protective or harmful, correct?

A Again, I have to know the context of what you're talk about.

Q We'll move on.

You're familiar with MedDRA, correct?

A I'm somewhat familiar with MedDRA.

Q Are you a licensee of MedDRA?

A No, I am not.

Q Do you have access to MedDRA license

through somebody?
A I have access to MedDRA through my work with Q Scan, FDA, and then also one of the guys at MedDRA gave me the MedDRA dictionary and then I'm also on the -- through National Library of Medicine one can get access to MedDRA.
Q How many levels to MedDRA are there?
A Lower level, preferred, higher level term five.
Q And a given -- putting low level terms out of the picture. The FDA does not code at the lower level term level, correct?
A I can't answer that. I'm not sure.
Q I'll represent to you that the FDA when you get the data is at the preferred term level and they don't provide it at lower level terms. Do you have any reason to dispute that?
MR. BARNES: Do you have any basis upon which to accept or reject Mr. Altman's assertion.
THE WITNESS: No, I don't.
Q Okay. MedDRA is a hierarchical classification; is that correct?
A Yes.
Q I believe the highest level is system organ class, correct?

publicly available that shows analyses that have been done at levels different than the preferred term?
A I don't follow every single thing the FDA does so I really couldn't say.
Q Have you ever done analyses using AERS at levels other than the preferred term level?
A Yes.
Q Do several preferred terms fall under one high level term?
A Sometimes.
Q Can they fall under more than one high level term?
A It's my understanding that each preferred term only maps up one way.
Q Then several high level terms would accumulate to one high level group term?
A Sometimes.
Q Can they go to more than one high level group term?
A No.
Q So, I mean, if we look at it, we have got a bunch of preferred terms. There's a high level term that's going to cover those particular preferred terms. Let's go from the time table.
You have a system organ class. There's

A That's my understanding.
Q Then you have high level group term underneath that, correct?
A I always mix them up. I have to look. Higher level term, higher level group term, preferred term, lower level term. I always mix them.
Q It's higher level group term and then high level term is my understanding.
Are you aware whether preferred terms can exist at more than one place in the hierarchy?
A It's my understanding that each preferred term is unique.
Q Do you know if the FDA does any comparisons using the MedDRA dictionary at levels higher than the preferred term?
A I am not privy to everything the FDA does. I wouldn't know.
Q Have you ever seen them do it at a higher level than the preferred term? I'm not asking do you know if they always do it. Have you ever seen it been done?
A The FDA does not release their protocol. I'm not sure what they do. There's a lot of people there.
Q Have you ever seen the FDA make anything

going to be a number of high level group terms under system of organ class, correct?
A Yes.
Q If we take any one of those high level group terms, there will be a number of high level terms that will exist under it, correct?
A Not necessarily, it could be one.
Q A number, it could be one or more?
A Sure.
Q If we go down to the high level term level, there will be one or more preferred terms under each high level term, correct?
A That's my understanding.
Q Do you think this is a -- is this a random -- strike that.
Do you know how many preferred terms there are?
MR. BARNES: Yes or no.
A Exactly, no.
Q Approximately?
A Yes. Approximately 30,000 plus preferred terms.
Q Is there- -- and MedDra is used by regulatory agencies around the world, correct?
A Not all of them.

Q Is it used by the FDA?
A It is used by the FDA.
Q Is it used by the Uppsala Monitory Center, the World Health Organization?
A I thought they used WHO-ART.
Q Is it used by the EMEA?
A I'm not sure.
Q Is the arrangement of preferred terms within MedDRA random?
A Is it random? I don't believe it's random.
Q Was there some body who tried to take these preferred terms and put them into logical groupings?
A Yes, I believe that there's a body that decided on the terminology and how it would -- how it would work.
Q So there's at least in some opinion if a given high level term has let's say five preferred terms underneath it, in that body's opinion there was a reason for putting those five terms under the same high level term, correct?
A I really wasn't privy to the design and development of MedDRA coding so I haven't studied it.
Q Have you ever read any of the MedDRA documentation that comes with the MedDRA license?
A Yes.

pharmacoepidemiologic study was done prior to its withdraw to support the withdraw of Fenfluramine and Dexfenfluramine?
A Yes, I'm aware of the literature.
Q So when you say aware of the literature, would you say there was a study?
MR. BARNES: Don't guess. If you want to look at the literature. Don't guess as to what happened. As long as you know. I'm just saying, as long as you know.
THE WITNESS: But, I mean, I really shouldn't talk about them, right, because I worked on the lawsuits?
MR. BARNES: Well, are you currently engaged in litigation consulting on Fenfluramine or Dexfenfluramine?
THE WITNESS: Not now.
MR. BARNES: Why don't you -- this isn't necessary to your examination rather than put her in a protection conflict or confidential relationship she has with parties who are not presently with us here today.
MR. ALTMAN: I mean, if she's aware of literature. I'm not asking for company internal documents. If she's aware of literature that was a

Q Do you know if there are any drugs that have been withdrawn in the absence of any placebo-controlled studies demonstrating an increased risk?
A Say that again?
Q Do you know if there are any drugs that have been withdrawn in the absence of any placebo-controlled studies showing an increased risk?
A Yes.
Q What drugs can you think of?
A One of them I can think of is Phenylpropanolamine.
Q Okay. Can you think of any others?
A Potentially Rezulin.
Q Are you familiar with Fenfluramine and Dexfenfluramine?
A Yes, I am.
Q Do you know if they were placebo-controlled trials for Fenfluramine and Dexfenfluramine --
A For approval, yes, they were.
Q I'm not quite finished -- that showed there was an increased risk of valvular heart disease?
A Clinical trials? I'm not aware of clinical trials that found that.
Q Do you know whether any

pharmacoepidemiological study?
MR. BARNES: You can answer that question.
A Yeah, I reviewed all the pharmacoepidemiology on those drugs.
Q Do you know that there was an announcement from the Mayo Clinic about three months before the drug was withdrawn?
A Yes, I'm aware of that.
Q Do you know what that announcement, in sum and substance, was about?
A I can't remember exactly to date, but yes, I remember the work that they did on working valvular heart disease.
Q If I told you that was the Mayo Clinic announcing that they had discovered a number of patients with particular kind of valvular heart disease, does that refresh your recollection at all?
MR. BARNES: Objection.
A Yes, I remember the study.
Q Was that a pharmacoepidemiological study?
A Which announcement?
Q The announcement from the Mayo Clinic about those particular case reports?
A The case report itself was not a pharmacoepidemiology study.

Q This was the announcement by the Mayo Clinic in July of 1997, correct?
A I can't remember offhand.
Q Did you do anything -- there were a number of charts that existed in various reports, the experience or other declarations that you reviewed, I think you've commented upon.
Did you do any independent review of that data to determine whether those charts are accurate or inaccurate? I'm not talking about interpretations of the data, which you may disagree with.
Do you have any basis for saying that a particular chart within the report was not correct, was wrong?
A For different charts in different reports, yes, actually I do say that some of them are wrong or inaccurate.
Q That the underlying data is wrong, that if it says there was a certain percentage, you've done review that says that it really wasn't that percentage?
A I've looked at some of the numbers and found some of the numbers, for example in the FDA report, are just wrong.
Q I don't understand what you -- the FDA report?

A The FDA says they did an analysis and this was the number of cases and this is the number of non-cases and the numbers are wrong based on what they said they did. Is that what you're saying?
Q I think we're talking about two different things. I'm not talking about FDA's analysis.
In Dr. Blume's expert report there were a number of charts which you comment upon in your expert reports, correct? In your original?
A In my original report, yes.
Q You've also done -- there were also some charts attached as part of a declaration by Dr. Blume, which you also reviewed for your supplemental report, correct?
A Yes.
Q And you commented upon those charts, correct?
A Yes.
Q Did you do, aside from its interpretation which I'm not asking you about, did you do any kind of a review of the underlying data to conclude that those charts are not accurate?
A I don't have to go to the underlying data in some of these charts to find that they're inaccurate because they're mislabeled. And that's what I'm

talking about.
Q Aside from mislabeling, have you done any of the work that says if at one point the chart said it was 6 percent that it wasn't really 6 percent?
A Can you show me where you're --
MR. ALTMAN: This isn't --
MR. BARNES: Well, did you actually go back. If Mr. Altman's charts that were put into Dr. Blume's report said there were 19 migraines in the fourth quarter of 1996, did you go back and recount the 19 headaches in the report that he attributes to being the fourth quarter of 1996? Did you do that sort of review of Dr. Blume's report?
THE WITNESS: No, I did not.
MR. BARNES: Is that what you were asking?
MR. ALTMAN: That's what I'm trying to --
Q So you have no basis to say that any of the charts, aside from mislabeling and aside from interpretation --
MR. BARNES: You're talking about numerical values.
Q Numerical values, do you have any basis for saying any of the numerical values in any of those charts are not inaccurate?
A I can't say that because I do an analysis

and I find the signal detection analysis and I find nothing and then there's a report that I believe you did the signal detection analysis and say there's something. So I've done the analysis with my numbers and I guess in some ways, yes, I do confirm those by doing my own analysis.
Q But you didn't actually take and try to replicate the charts exactly as Dr. Blume has them in her report, correct?
A No, I did not go to the raw data and give clinical judgment as to any of the data that she did.
Q I'm not talking about clinical judgment. I'm talking simply the fact that you didn't go to the chart as Mr. Barnes said and if Dr. Blume has in her report that there were 19 reports of migraine in the fourth quarter of 2003, do you have any basis for saying that there were not really 19 reports of migraine in the fourth quarter of 2003?
A I did not go and replicate her work, no.
Q So you have no basis for saying that any of those charts are inaccurate, other than some disagreements of interpretation or labelings; is that correct?
MR. BARNES: Other than what's stated in her reports.

Q Correct. You didn't use the same tool, you used a different tool than what Dr. Blume used, correct?
A I believe so, yes.
Q And if Q Scan did some things one way that was different than what Dr. Blume requested, you could see different results that may be because of the method that was used and having nothing to do with the accuracy of the computation, shall we say; is that correct?
A No, that's not correct.
Q Okay. How is that not correct?
A I did data mining. Dr. Blume didn't do data mining.
Q Let me give you a different example.
We talked about the date issue before. What date to attribute to a particular report and you were not aware how Q Scan dealt with the multiple versions of a report; is that correct?
A They do the last best case for the data, but all the data is retained.
Q I understand that, but when you do data mining, you only want to use one -- you only want to count a report one time, correct?
A That's correct. That's why they do that

last best case so each report is only counted one time.
Q But if the last best case was six years after the FDA actually learned about a particular term; isn't that not accurate?
A I don't believe that they used the last date. I believe they used the first date of the report. But I would have to go back and verify that. I thought I did that earlier.
Q I'm sorry. If the first date of the report didn't contain the term and it only showed up in the last best case, wouldn't that also be inaccurate?
A Not necessarily.
Q But it could be. You wouldn't know, right?
A Such as the nature of data mining.
Q Correct. So you don't know what influence that might have on the report, correct?
A These are all such hypotheticals. It's hard to put this into any meaningful context.
Q What I'm getting at is if Q Scan used one mechanism for attributing the date, which was different than what Dr. Blume used, you could see different results based upon that, correct? Without either one of them being wrong?
A That's assuming that we did the same thing, which we did not do.

Q Understood. But if you did the same thing and you used different ways of assigning the date, you could see different results without either one of them being wrong, it's just the convention that was selected; is that correct?
MR. BARNES: Objection. Vague. If you can answer that.
A In the hypothetical situation that we actually both did the same thing, which we didn't do, any change in protocol or use of different data could get different results.
Q Okay. Have you ever designed a clinical trial?
A No.
Q Have you ever done the power calculations -- are you aware what power calculations are typically done with the design of a clinical trial?
MR. BARNES: We covered this in some significant detail last year. So with Dr. Weiss and Mr. Fromson and you, so you should ask a new question. That was covered in great detail a year ago.
MR. ALTMAN: I'm sorry. It was 10 months ago and I have some questions that are relevant to this and she rendered some new opinions so.
MR. BARNES: Ask a different question and

we'll go forward. She was asked for probably an hour's worth of questions on power calculations last time.
MR. ALTMAN: Are you going to instruct her not to answer?
MR. BARNES: That last question was asked and answered. You can ask another question.
MR. ALTMAN: I'm asking that question.
MR. BARNES: Ask it again. What's the question?
Q Are you aware that power calculations is typically done with the design of a clinical trial?
MR. BARNES: Answer that question.
A Yes, I am aware that they typically do clinical trial power calculations.
Q What is the purpose of doing those power calculations?
A The purpose is to estimate how many people they will need to enroll to complete the study.
Q Is that -- to complete the study but to see or not see a particular effect, correct?
A That's the whole -- whatever the purpose of doing the study is.
Q And the study that's not adequately powered may fail to see an effect even though it actually exists, correct?

A Well, the whole idea of doing this study is to see a clinically significant effect, so usually if it's not feasible to get adequate sample size, you wouldn't do the study.
Q I understand that. But if you don't have enough power in the study to see the -- to see a particular effect, you may not observe it even though there really is an effect, correct?
A You probably will have a point estimate but your confidence intervals will be too wide to have a statistically significant effect.
Q Is it also possible you may not see an effect at all because there isn't enough people in the study?
A Then why would you do a study in the first place. I don't understand.
Q Let's say you're looking for -- you're not looking for an effect, but to see an adverse effect that is very rare. If the study is not adequately powered, you may not actually see an effect, even though there actually is an effect, correct?
A Clinical trials are typically not designed to look at rare adverse events.
Q So the absence of a rare adverse event in the clinical trial doesn't really speak whether there

need to have this discussion.
MR. BARNES: You're not going to ask the same questions over and over again. Use the supplemental report. If you have something directly to the supplemental report, fine.
You've asked her hypotheticals. You've asked her what if it's 1 in 10,000, what if it's this, what if it's that.
Again, I'm not trying to limit you. Her testimony -- your firm has had the opportunity to question her on this exact point and you did and so, you know, I would appreciate your asking a different question other than what was covered in the last deposition.
MR. ALTMAN: I'm sorry, Rick, I need this in the context of my examination. If you're going to instruct her not to answer, go ahead and do that.
MR. BARNES: Ask the next question.
MR. ALTMAN: I've asked the question that's on the table.
MR. BARNES: Ask it. I want to hear it again.
BY MR. ALTMAN:
Q And if you did not see an adverse effect, this was in the context of the clinical trial that -- I

is -- that drug causes that particular adverse event, correct?
A That's reverse logic from my standpoint if you --
Q If an event happens one in a thousand patient years and you have five patient years of exposure, would you expect to see even one of those adverse events in that clinical trial?
A Based on probability theory, the probability would be very low.
Q And if you did not see an adverse effect, could you make a conclusion as to whether the drug causes that adverse effect or not?
MR. BARNES: Counsel, at pages 210 to 216 you went over this exact hypothetical and your counsel. And you were scribbling down the questions for Mr. Fromson.
I want you to look at page 210 to 216. You went through this exact same examples. She's not here to be re-examined on areas in which you've actually spent sufficient time covering. If you have a new question.
MR. ALTMAN: Rick, I'll point out to you she is cross noticed in Crone which is a new case. And I can ask her anything from start in Crone. We don't

have to go back.
If an event happens one in a thousand patient years and you have five patient years of exposure, would you expect to see even one of those adverse events in that clinical trial? Your answer was based on probability theory, the probability would be very low. And if you did not see an adverse effect could you make a conclusion as to whether the drug causes that adverse effect or not? That's the question on the table.
MR. BARNES: If you have an opinion on that, you can answer that question. Do you understand the question?
A It's an odd question. I wouldn't even think that way. The issue is if you see something, what does it mean. Not what does it mean to not see something.
Q Okay. So then would it be -- in that particular context, would it be a fair statement to say that because I did not see that adverse event that proves that the drug cannot cause that adverse event?
MR. BARNES: Objection. Vague. You may answer.
A It shows that there is no evidence for that event.

MR. ALTMAN: Objection. Nonresponsive.
MR. BARNES: Objection to the colloquy. Ask the next question.
MR. ALTMAN: Objection. Nonresponsive.
Q In that particular context, would it be a fair statement to say that because I did not see that adverse event that proves that the drug cannot cause the adverse event?
MR. BARNES: Objection as to fair, vague. You may answer.
A I wouldn't say that as a pharmacoepidemiologist. That's just not something I would say.
Q That wouldn't be a true statement, would it?
MR. BARNES: What?
A It's just not accurate.
Q Okay. That's fine.
MR. ALTMAN: I think we have five minutes left on the tape. This is a good a time to take a break as any. I don't know how long you need. I'm staying here, so.
MR. BARNES: Why don't we go off the record and take a short lunch break and be back between half an hour, 45 minutes. Depending how long it takes.

had any opportunity to evaluate any of Dr. Weiss Smith's analyses.
MR. BARNES: Well, I disagree that you've had no opportunity to evaluate Dr. Weiss Smith's analyses and we'll take your request under advisement and we will respond following the deposition.
MR. ALTMAN: That's fine.
BY MR. ALTMAN:
Dr. Weiss Smith, I wanted to ask you briefly about the Society of Epidemiologists. You are a member?
A Yes.
Q You are a fellow?
A Yes.
Q Are you on the board?
A I have been on the board.
Q Is that the main conference for pharmacoepidemiologists worldwide?
A It's the main professional association for pharmacoepidemiologists, yes.
Q And they have basically an annual meeting every year, correct?
A They have an annual meeting, a mid-year meeting. A few others.
Q At the annual meeting there's typically

THE VIDEOGRAPHER: Going off the record. The time is 12:43 p.m. This is the end of tape number 3.
(Break for lunch.)
THE VIDEOGRAPHER: We are on the record, the time is 1:42 p.m. This is the beginning of tape number 4.
BY MR. ALTMAN:
MR. ALTMAN: Before we continue, I just want to put something on the record with respect to the Q Scan system. At Dr. Weiss Smith's first deposition and at this deposition and in her report she made extensive use of the system from a third-party vendor called Q Scan.
We have not had an opportunity to evaluate the Q Scan system. We don't have an opportunity to run inquiries on the Q Scan system and to evaluate what other kind of analyses could have been done on the Q Scan system and we have asked to be provided access in a similar capacity to that which has been made available to Dr. Weiss Smith.
At this point we have not been provided with that capability and have requested that be provided that capability and we'll have to resolve that issue going forward. But as of this point we have not

lots of posters presented, correct?
A There are quite a number of posters.
Q Those posters are submitted to the society for review by its members to decide whether it should be -- the poster should be posted at the annual meeting, correct?
MR. BARNES: Objection. Assumes facts not in evidence, if you know. The abstracts are reviewed by volunteers among the membership and they are scored and then evaluated for potential to go into oral presentations and/or posters.
Q As you said, some of those posters are selected for oral presentations, correct?
A Some of the abstracts are selected.
Q Some of the abstracts are selected for oral presentations, correct?
A Some of them are.
Q There's a much smaller number of oral presentations than there are posters, correct?
A Yes, the number of oral presentations is limited.
Q And you've given oral, you've given oral presentations at asbe (phonetic), correct?
A Yes, I have.
Q It's a different group of people who select

abstracts for -- strike that.
It is not the same group of people who select the abstracts that will be allowed to have oral presentations as grade the abstracts, correct?
A That's not exactly true. There's a lot of overlap.
Q There's a lot of overlap. But it's not the same thing. When the abstracts are scored by the reviewers do those people, as part of that scoring, decide whether they should be an oral presentation or not?
A All the abstracts and all the scores goes to the scientific committee at mid-year.
Q Okay.
A They determine along with the committee in charge of the meeting what is going to be presented, what are the topics, what sessions are going to be run and what's going to be in the different sessions.
Q That will then decide which abstracts should be accepted for oral presentations, correct?
A That's typically where they make most of the decisions. Not the final decision but the recommendations.
Q I'm not going to mark it as an exhibit, but I know that you have it. I'd like you to go to your

Q And 2001?
A Again, about the same as 1999.
Q Which was?
A About 2000.
Q And in 2002?
A About 2,200.
Q Now in 2003, how many in 2003?
A Oh, just under 3,000.
Q Would it be, based on what you see here, would it be an unreasonable approximation to say that there probably was about 1,500 reports in the first half of 2003?
MR. BARNES: Objection. Calls for speculation.
A Based on this scale you can't tell what happened in any one quarter. This is full year.
Q I understand, but given the trends of what you see there, do you expect that it was more -- that it's probably about half the number of reports?
MR. BARNES: Objection. Asked and answered. You may answer.
A You cannot say anything because these reports don't necessarily come in random order. So no, I wouldn't speculate in one quarter or the other based on an annual total.

original report for one second.
MR. BARNES: That's an exhibit in the prior deposition. Do you recall which deposition exhibit it was?
MR. ALTMAN: I believe it was Deposition Exhibit 1.
MR. BARNES: So referring to Exhibit 1 from the prior deposition.
Q I'd like you to go to page 16 of your report. Do you see that?
A Okay.
Q It's a little bit difficult with the scale but in 1998 can you tell me in the top chart which is entitled GABA Benton Spontaneous Reports, can you tell me how many reports there were in 1998, and I'm not asking you for precision. I'm asking you within the scale of your chart as you do it there, approximate number?
A In 1998?
Q Yes.
A Somewhere between 500 and 700.
Q Okay. And in 1999 approximately how many?
A About 2000.
Q In 2000 about how many?
A Approximately 1,500.

Q Taking a look at the bottom chart entitled total prescriptions?
A Okay.
Q About how many in 1998?
A 4 million.
Q And in 1999?
A Just under 8 million.
Q In 2000?
A Looks like 10 million. Slightly more.
Q In 2001?
A A lot of zeros here. More than 12 million prescriptions.
Q When you say more than 12 million, can you be a little bit more precise than that?
A It's a big box in a little chart, so.
Q Well, the line above is 14 million, correct?
A It's more than 12 million, it's less than 13 million, how's that.
Q That's perfectly fine. In 2002?
A Slightly more than 14 million.
Q And in 2003?
A It jumps to 16 million.
Q Now, with this chart do you think you'd be in a better position to estimate whether about how many

prescriptions there were in the first half of 2003?
MR. BARNES: Objection.
A Again, I wouldn't speculate within a full year how that goes. If there's seasonal variations or if it's increasing over time. So no.
Q Do you ever do interpolation between data points?
A I try not to. I like to work with the data that I have as opposed to doing prediction.
Q Do you have any knowledge that would suggest that there is something that happened in 2003 that would say that it's not a pretty smooth usage throughout 2003?
MR. BARNES: Objection. Calls for speculation.
A I don't have any basis to comment on your question.
Q So you don't -- I'm just asking, do you know of anything that might have caused there to be a change in prescribing patterns in 2003?
MR. BARNES: Objection. You may answer.
A I don't remember the timeline of the different indications. I know it had some additional indications, but I just don't remember the timeline.
Q If they were -- if the new indication was

recognition of an unusual or unexpected pattern of events or a pattern of events that is consistent with a biologically plausible explanation either within a single case or across a series of cases. Do you agree with that statement?
MR. BARNES: Would you read it again more slowly.
Q Pharmacovigilance is dependent on astute clinical recognition of an unusual or unexpected pattern of events or a pattern of events that is consistent with a biologically plausible explanation either within a single case or across a series of cases?
A I agree with the sentence but I do not believe it's complete.
Q As in I didn't read the whole sentence or that --
A It's not a complete description of what pharmacovigilance is.
Q Okay. The next sentence, "Such clinical pharmacological knowledge-based approaches have been referred to as traditional methods of signal detection." Do you agree with that statement?
MR. BARNES: Objection.
A Say it again.

in the 2001/2002 time frame, does that help your recollection?
A The one thing I see is in 2003 between 2003 and 2004 the generic drug was approved and quite quickly dominated the market.
Q Going back to the spontaneous reports. Do you know of any events in 2003 that could have caused a change in the adverse event reporting associated with Gabapentin or Neurontin?
MR. BARNES: If you want to look at your report, go ahead because you've not reviewed your report as extensively as your supplemental, so.
MR. ALTMAN: I just asked.
MR. BARNES: I know, but this is discussed in her report. Perhaps if you want to look at the report, that's fine.
Q As you sit here right now, do you know?
A There are constantly things going on that change and affect reporting rates. It is absolutely not static and the use of the drug increased substantially. It's used in different indications. There's a lot of things going on.
Q Okay. I'm going, I want to read to you a statement and see if you'll agree with the statement. Pharmacovigilance is dependent on astute clinical

Q Such clinical pharmacological knowledge-based approaches have been referred to as traditional methods of signal detection.
A I'm not sure I agree with that.
Q Okay. I'd like to read you another statement. We can data mine on Gabapentin but I don't think that negative data mining findings would make a strong counter-argument to a signal that may have arisen from clinical observations.
A Can you please put that in context?
Q You can agree or disagree with the sentence?
MR. BARNES: Objection. She's asked you to -- can you answer the question as stated. If you agree or disagree. If you can't, you can't.
A Can you repeat it?
Q Sure. We can data mine on Gabapentin but I don't think that negative data mining findings would make a strong counter-argument to a signal that may have arisen from clinical observations.
A To really answer that I need to understand the context in which it's said. It doesn't make sense standing alone.
Q If a person concludes that there was a signal without using data mining and then you go and do

some data mining and for the data mining you don't see a signal, does that mean that the person, the clinical reviewer, was wrong when they thought there was a signal there?

MR. BARNES: Objection. If you know.

A Data mining is a signal of disproportional reporting. There's a lot of reasons why things may signal that are true may signal and things that are false may signal and vice versa. I don't understand --

Q So I think what -- I let her finish. Did you finish your answer?

A I don't understand how you're putting these two things together, data mining and --

Q I received a -- I'm in pharmacovigilance for a pharmaceutical company and I've received a number of case reports that I believe constitutes a signal, okay, I decide that I need to do some followup along those lines.

One of the thing I choose to do is some data mining. When I do the data mining I don't find any signal in the data mining. Does that mean there's no signal that -- from my clinical judgment?

MR. BARNES: You're a doctor? The person doing the data mining, the person that's doing the pharmacovigilance --

MR. ALTMAN: I'm in pharmacovigilance, it doesn't matter.

Q The person working in the pharmaceutical company in the pharmacovigilance department has concluded based on case reports that there is a signal. If you then go do some data mining and you don't see any signal in the data mining, does that mean the person was wrong?

A I don't know.

Q Okay. So the absence?

A From what you've given me, I don't know. I don't know -- it's going to depend on the circumstance whether what they think is a signal ends up being a true association or not or causal or not. That's a long way off from what you're asking.

Q But the absence of a signal in data mining does not mean everything is a okay; is that correct?

A That can be the case. Not everything will signal in data mining, it's only proportional reporting.

Q That's all I'm trying to get at.

Dr. Weiss Smith, I'm going to hand you a document, I'm not going to mark it as an exhibit -- it was marked. We can mark it if you want. I only have one copy?

MR. BARNES: Let's try to mark it.

MR. ALTMAN: I only have one copy.

MR. BARNES: I can do that quickly.

MR. ALTMAN: Okay.

MR. BARNES: Two seconds I'll get this copied.

MR. ALTMAN: I don't need a copy. If you want to just mark that one.

MR. BARNES: Let's mark this one as the next exhibit in the deposition.

(Whereupon, a document was marked as Deposition Exhibit Number 22.)

(Witness reading.)

Q I just want you to take a look at that quickly.

MR. BARNES: The date on it, let me say what it is for the record. It's a printout, Serious Adverse Events, Gabapentin Related Clinical Studies cases 1/1/1980 to 31/12/2003.

Q Which is the European date?

MR. BARNES: Yes.

Q It appears to be run on 5th of February, 2004, correct? If you look all the way on the right-hand -- all the way on the right-hand side?

MR. BARNES: Yeah.

Q It's also marked as Pfizer, underscore, THO, underscore, 00007 -- I'm sorry, 793.

MR. BARNES: Thank you. That's good enough.

Q I'd like you to go to page four of the document. First of all, does this appear to be a listing of serious adverse event reports from the Gabapentin related clinical studies cases?

A That's the title.

Q Okay. On page four, the second item down, do you see that one? It's a got number of 001-0945-9600035. Did I read that correctly?

A Which number down?

Q The second report. I'm sorry it's --

MR. BARNES: Is it the one --

Q I'm sorry, it's the third page of the document.

A The second report down? Say the number again.

Q Under the event term, it says psychosis, are we talking about same page now?

MR. BARNES: 0010945960035. Is that the one?

Q Yes, do you see that one there? It should be the second one on the page. Did I read that report

number there correctly? Did I read that report correctly?

A Rick just did.

Q I just want to make sure I read it correctly. Did you review this adverse effect report, this MedWatch report?

A No. I didn't.

Q Under country it says USA, did I read that correctly?

A Okay.

Q Under sex it says M, correct?

A Yes.

Q And that would appear to mean male. Is that a reasonable interpretation, even though it doesn't appear to be indicated in the chart?

A There's no key, we can make that assumption I guess.

Q Under age it says 26?

A Okay.

Q Under weight it says 58.5-kilogram, correct?

A That's what it has here.

Q And event onset date, it 434?

A 434, yes.

Q Under event term it says psychosis,

causality in this context, that is what the clinician wrote.

Q And you have no basis --

MR. BARNES: Let her finish her answer.

A My caveat is I want to be very clear that this causality assessment is not the same as saying this -- the drug and the event were causally related from an epidemiologic point of view.

MR. ALTMAN: Objection.

A This is very narrow.

MR. ALTMAN: Objection to everything after my caveat is as nonresponsive.

MR. BARNES: Don't worry about it. That's meaningless. Go ahead.

Q You have no basis to conclude that this patient did not have psychosis, correct?

A That's a clinical judgment that I don't feel qualified to make.

Q But even if you were qualified, there is -- is there sufficient information on this line item here for you to question whether this person actually had psychosis or not?

A There's not enough information here to make a clinical judgment.

Q Other than somebody made a clinical

correct?

A Okay.

Q And the action taken, it says permanently discontinued, correct?

A That's what it says here also.

Q And under investigator causality it says related, correct?

A That's what they wrote.

Q You have no basis, as you sit here, for questioning whether the investigator thought this was causally related, do you?

MR. BARNES: Objection. The word causally related. It says related. But go ahead.

A There is a great difference between the causality assessment that clinicians do in this context and what we consider causal in the epidemiologic context.

MR. ALTMAN: Objection. Nonresponsive.

Q Do you have any basis for questioning whether the clinical investigator said causality related?

MR. BARNES: Objection. She was asked that question.

A I thought I did answer that. It says here investigator causality related. So however they define

judgment that it was psychosis, correct?

MR. BARNES: Objection. If you know.

A I don't know how they labeled the term.

Q This document came out of the company -- this document was produced by the company?

A Right.

Q Somebody at the company put down psychosis for this, correct?

A Probably not.

Q Who do you think put down psychosis?

A Most likely the clinical investigator or someone in their staff wrote that.

Q That would be a doctor presumably, correct?

MR. BARNES: Objection.

A Probably somebody clinical, not necessarily the doctor. It could be a study nurse. It could be anything.

Q And that person is a clinician, though, correct?

A I don't know. I don't have -- I don't have anything to base that on.

Q Okay. That's fine. You can put that document aside.

All right. The moment you thought we'd never get to. Why don't we pull out your report.

Do you have your supplemental report in front of you?
A Now I do.
Q I believe it's Exhibit 18; is that correct?
A Yes.
Q Opinion one you say FDA conducted a meta-analysis of clinical trial data across 11 antiepileptic drugs. Did I read that correctly?
A That is correct.
Q In my review of FDA's report the transcript of the FDA advisory committee meeting and other related materials have found that there was inadequate bases to reliably assert that Neurontin was associated with suicidality. Did I read that correctly?
A Yes.
Q Pfizer was correct in concluding that based upon the available data there was no signal for suicidality with Neurontin. Did I read that correct?
A Yes.
Q I think we defined that association and signal are not the same thing, correct?
A That is correct.
Q So is that last sentence of your opinion there, is that related to the sentence before which is talking about association or is that a completely

committee, based on all of the available data that they looked at, there was no statistical association, there was no signal of disproportional reporting, there was no significant -- I already said that statistically significant elevation.
Therefore, there was nothing for them to make a hypothesis that with clinical relevance that Neurontin would be associated with suicidality.
Q The advisory committee hearing, did they discuss post-marketing safety data?
A Did they discuss it? I'd have to go back in the transcript. But I believe there was some information in the report.
Q But you're talking Pfizer was correct in concluding that based upon the available data, there was no signal for suicidality with Neurontin and that's where I'm confused.
You just were talking about the FDA did an analysis purely of clinical trial data and it was only a statistical analysis, correct?
A Yes.
Q So you're limiting your opinion there to whether the statistical data demonstrated a signal; is that correct?
A If you don't have an association that's

distinct sentence?
A It's distinct.
Q When you use the term there, no signal for suicidality with Neurontin, are you using that in the context of a data mining perspective as we discussed earlier?
A No, this is a different context. This is the context of what the FDA advisory committee use of the term signal.
Q You say Pfizer was correct in concluding that based upon the value data there was no signal. That's not the FDA's conclusion, is it?
A Excuse me.
Q Your opinion here was Pfizer was correct in concluding that based upon the available data there was no signal for suicidality with Neurontin?
A People throw around the term signal. And we defined it in the context of data mining, we talked about an alert. We're no longer talking about context of data mining here; is that correct?
Q You wrote -- this is your opinion, I don't know what you mean?
A The advisory committee kept going back and forth and saying is there a signal, is there a signal, is there a signal. I'm saying, within the advisory

higher than not having a signal. A signal is more of a hypothesis.
Q So you could have a signal and later there's no association found, correct?
A That's correct.
Q Here's what I'm totally confused about. You say Pfizer was correct in concluding that based upon the available data. So you're talking about Pfizer's conclusion that there was no signal. That sentence has nothing to do with whether there was an association, correct, we discussed that before?
A Opinion one is specifically talking about the meta-analysis and the information there. I have separate opinions for the different types of data.
Q So when you say Pfizer was correct in concluding that based upon the available data there was no signal with supplemental report for Neurontin, that opinion is limited to a statistical analysis of the data, correct?
A Not limited to a statistical analysis.
Q Well, did FDA do any other analysis, other than a statistical analysis?
A But it's not just the analysis.
Q What else is there?
A It's also the interpretation of the

analysis.
Q Okay. But at its core the FDA didn't discuss open label studies, correct?
A The FDA based their analysis on the control clinical trials.
Q Correct. So your statement here is limited to the analysis of the controlled clinical trials or any interpretation of that analysis, correct?
A Yes, in this opinion I'm specifically limiting it to the meta-analysis and all the associated documents with that one, yes.
Q So you're not saying here that there might not have been a signal from other source or some other way that Pfizer might have known about it, correct?
A The rest of my documents do talk to that, that there is no signal in the epidemiologic literature, in the spontaneous reports. Specifically here I'm addressing that one issue.
Q When you say there's no signal, that's limited to an alert plus clinical data, correct?
MR. BARNES: Clinical relevance.
Q Clinical relevance, I'm sorry.
A For the data mining.
Q Well, you say -- when you say that there was no signal in the spontaneous data, that's based

A Yeah, Exhibits 19 and 21.
Q I'd like you to go to page 16.
A (Witness complies.)
Q In your review of the FDA materials, did you see any evidence that the FDA took off-label use of any of the drugs into consideration in evaluating the data?
A Say that again.
Q In reviewing the FDA materials, when I say the FDA materials I'm talking about, you know, based upon the alert, did you see any evidence that the FDA reviewed the information in the context of off-label use of the drugs -- strike that.
Do you know what the term off-label use means?
A Yes.
Q You're aware that many of the drugs that -- were the subject of the FDA alert were used off-label, correct?
A It's my understanding.
Q Are you aware that approximately 80 to 90 percent of the usage of Neurontin is for off-label purposes?
MR. BARNES: Objection.
A I did not have the exact figures on

upon data mining, correct?
A In the spontaneous reports, data mining and the evaluation of the safety summaries from the company, relying on those also.
Q On the safety summaries you're talking about are those that were done in conjunction with the new drug application?
A They're in my first list of exhibits.
Q Just take a brief look at them. I don't see listed in your materials here periodic reports. Did you review any periodic reports in this case? You know what I mean by periodic reports, correct?
A Yes, I do. That I don't recall.
Q I don't see any listed here, so if -- I'm assuming that you did not review periodic reports?
A Whatever I relied on I gave you.
Q You just said relied on or reviewed. Is there any material that you reviewed that is not on this list here?
A I don't believe so.
Q So this should be the complete list of everything you looked at in this case, correct?
A I believe that it is.
Q When I say this, I mean this plus the new supplemental report?

off-label use for Neurontin but I recently read that bi-polar disease is very commonly treated with drugs that are not prescribed -- that are not labeled for it. So there's a lot of off-label use in that condition.
MR. ALTMAN: Objection. Nonresponsive.
Q At the time of the -- do you have an understanding of whether labels are written for the indication in which the drug is going to be approved?
A It's my understanding that the labels are very specifically written and the studies, clinical studies, are done for the indication for which the drug is being approved.
Q At the time -- do you know when the Neurontin was first approved?
A I believe it was '93 or '94. Right in there.
Q Do you know what the indication was at the time it was approved?
A I know it was for epilepsy in adult but I don't know the specific subtype of epilepsy.
Q If I told you it was adjunct therapy for seizure control, does that refresh your recollection?
A No, but I know it was for adults.
Q In 1994, do you know whether there were any clinical studies that had been done on bi-polar

patients?
A I don't know the dates when they started doing the other studies, no.
Q I'll represent to you there were no studies of bi-polar -- there was no specific study of efficacy for bi-polar at the time of the original approval. At that point in time what did the company know about the safety of Neurontin for use in a bi-polar population?
A At which time?
Q At the time of the original approval?
A At the time of the original approval I don't know what the company knew about the safety of the drug for other indications, other than the ones that they studied.
Q Would it be a scientifically valid statement to say that the drug was safe for use in a population which had never been studied?
MR. BARNES: Objection. From a clinical point of view or in terms of epilepsy?
Q From an epidemiologic point of view.
MR. BARNES: If you have an opinion. You don't have to have an opinion.
A The benefits and risks of each treatment need to be considered within the context. That's my opinion.

Q If the drug had not been studied for a particular use, what do you know about the risks associated with using it in those patients?
A Personally me, I'm not a clinician.
Q What would the company have known?
MR. BARNES: Objection. If you know.
A I don't know what the company knew when it was approved.
Q If they had never studied it in a bi-polar population, could they have responsibly said it safe for use in bi-polar population?
MR. BARNES: Objection.
A Potentially.
Q What would be the basis?
A Basis on the safety data that they did collect in humans and of course the animal studies. So they know what the risks are. It's a question of balancing those risks against a different disease state.
Q So even though they weren't never tested in that population, you could automatically extend everything they knew about one population to another?
MR. BARNES: Objection.
A That's not what I said.
Q Were you aware that Pfizer pled guilty to

crimes? And when I say Pfizer, I mean Pfizer, Warner-Lambert, Parke-Davis, this entity?
MR. BARNES: Objection. That was asked at the prior deposition, Counselor. Do you want to just, you know, put it in the context of this case.
Q Were you aware of that?
MR. BARNES: If you were aware.
A Yeah, I heard about it.
Q Were you aware one of the items that was pled guilty to is that the drugs lacked adequate instructions for use in off-labeled populations?
MR. BARNES: Don't answer that yet. Repeat the question, please.
Q Were you aware that one of the items that was pled guilty to is that the drugs lacked adequate instructions for use in off-label populations?
A No.
Q As part of -- would you consider yourself knowledgeable on good pharmacovigilance practices?
A I'm not an expert on good pharmacovigilance practices, no.
Q Do you think it's important as part of your pharmacovigilance practices to look at the populations that are actually using your drug?
A That's part of the guidance document from

the FDA, yes.
Q Do you agree with that?
A Yes, I do.
Q So if a company knows that a population is using their drug in substantial numbers that's different than what they studied in the clinical trials, should the company take steps to specifically look at that population's adverse events?
MR. BARNES: Objection. Vague. Overbroad.
Q You can answer. Unless you don't understand?
MR. BARNES: If you have an opinion or you don't understand.
A I don't know. Say it again. Maybe I can --
Q If a company becomes aware that a substantial portion of the use of their drug is in an off-label population for which they have not performed little, if any, studies. Should the company take steps to specifically monitor the safety of the drug when used in that particular population?
MR. BARNES: Objection. She's not expressed any -- named as an expert in the company's conduct of pharmacovigilance. So if you have formed an opinion separate from this engagement, you can answer.

But you've not been asked to do so in this case.
A From my perspective the companies do pharmacovigilance regardless of indication. They look at all events that are reported to them.
Q I understand that, but do you think they should separate out the events from one indication versus another indication to see if there are differences or disproportional reporting between those indications?
MR. BARNES: Objection. Beyond the scope of her report. Overbroad if you haven't formed the opinion, you don't have to give an opinion on it.
A I don't have an opinion about how they should conduct their pharmacovigilance in that regard.
Q Bottom of page 16 you say, I am not aware of the FDA's grading all or parts of NDAs like an examine nor summarily rejecting an NDA based on errors, omissions or inappropriate methods with this one section. How many NDAs -- first of all, did I read that correctly?
A Yes.
Q How many NDAs have you reviewed while at the FDA?
A I never had to review a completed NDA.
Q How many post-marketing safety sections of

an NDA did you review while at the FDA?
A I don't do clinical reviews. Those are done in the review division.
Q How many, I think I asked this, you've not ever developed a post-marketing safety section of an NDA, correct?
A That's correct. But nothing I've heard of, discussed, nothing I've learned in any of my regulatory courses had anything to do with how the FDA grades an NDA or sections of it. I've never heard of that.
Q You say nor is there any evidence that the FDA accepted their methodology. What is your basis for that statement?
A What I understand is the FDA does their own analysis.
Q That's based on general instinct, but you've not actually done that analysis, correct?
A No.
Q Have you ever spoken to anybody at the FDA and asked them what they do with the post-marketing safety surveillance section provided to them by a manufacturer?
A We have talked about it. I've looked at some of them in legal cases, other legal cases. I've worked within a review division for some period of my

time there so I'm familiar, somewhat, with what they at least in the past have done.
Q Do you know if the FDA has ever gone back to a manufacturer submitting an NDA and asked them to do additional analysis in their post-marketing section?
A Yes.
Q Page 17. Are you aware of any times that a black box has been required for a drug without an epidemiologic study of some kind?
A Could you say that again, please.
Q Sure. It's a bad question.
You said this gives the FDA the regulatory authority to require a boxed warning based on animal data alone when human data are not available.
Did I read that correct?
A Yes, this is directly -- and the quote is directly taken from the CFR.
Q I understand. Thus in some situations the FDA may decide to warn about a particular risk identified in animal data even if there is no evidence that is applicable in humans when they believe that such a warning will serve the public health. Did I read that correctly?
A Yes.
Q Do you know of any times when the FDA has

required a black box without animal data and without --
MR. BARNES: Without animal data.
Q Without animal data and without epidemiology or epidemiologic studies?
A Do you include clinical trials within epidemiologic studies?
Q Yes.
A So you're saying a black box warning with no human data and animal data.
Q No, based on post-marketing?
MR. BARNES: Why don't you ask your question.
Q Do you know of the FDA ever required a black box based solely upon case reports?
A I believe they did for Felbamate. There's one example. It had a very rare and unique adverse event.
Q What about Fenfluramine?
A Fenfluramine.
MR. BARNES: If you know.
A I'm not really sure.
Q What about Baycol?
A I'm not up on that one.
Q Section C. Last sentence, there is ample evidence in this case that FDA would only consider

randomized clinical trial data to assess whether AEDs are associated with supplemental report?

MR. BARNES: Page?

Q Same page.

A Right here.

MR. BARNES: Reading. I'm sorry. Go ahead.

Q What is the basis of that sentence?

A The basis of that is if you go and look at the transcript, you'll see Katz very specifically say that we couldn't use the data from the spontaneous reports and they specifically ask the companies not just for clinical trial data but for the placebo-controlled, the controlled clinical trial data.

Q Okay. Page 18. By the way, 201.57(e) here, which version did you use?

A 201.57.

Q Page 17?

MR. BARNES: If you know.

A I think it should be in the reference list. I tried to be very specific.

Q I think you say here the April 1st, 2008 edition, correct?

A I'm looking.

Q The first item?

issues.

Q Are you aware that there are certain obligations and certain times that the company must change the label?

A Like I said I'm really not an expert on that regulations for labeling.

Q Okay. So when you quote Dr. Blume, it is not universally necessary to employ the various methods of epidemiology to establish whether there's an association between a drug and a risk. That association there could be in the context in which the FDA uses it within the regulations, correct?

MR. BARNES: Objection. Vague. Lack of evidentiary foundation.

A All I'm saying here is that in Blume she misquotes and misstates what the Federal Register actually says.

Q Federal Register or Federal Regulations?

A Code of Federal Regulations.

Q Bear with me a second here. Let's make sure we get this right.

In the CFR prior to the changes in 2006, the sentence says --

MR. BARNES: Wait, changes prior to 2006?

MR. ALTMAN: Prior to June of 2006 the

A Yes.

Q Were you aware there was substantial changes to section 201 in June of 2006?

A I didn't go into a historical evaluation, no. I just looked at the most recent version.

Q In 2017.57(e) I think we discussed this earlier whether a statistical association was required in order to change the label, do you remember that earlier?

A Excuse me?

Q Do you remember discussing earlier whether a statistical association was required in order to change a label?

A That was one of the questions you posed to me. Yes, I do remember that.

Q You said you did not think you had to have a statistical association to change the label; is that correct?

A Based on what I read, FDA has quite a bit of discretion on what it is that they can use as a -- evidence to ask for a labeling change.

Q What about for the company to change the label?

A I'm not as familiar with what the company's rules are for labeling changes and the regulatory

language changed.

Q Part of the regulation says: In accordance with 314.70 and 601.12 of this chapter, the labeling must be revised to include a warning about a clinically significant hazard as soon as there is reasonable evidence -- I'm sorry, I'm reading the wrong one. Strike that. Let me read you the correct one.

MR. BARNES: You may want to just -- you may want to have her read it rather than read it to her. It's very difficult to follow reading it. Try your best. We can pull it for you, if you want.

Q The labeling shall --

MR. BARNES: Would you tell me what you're reading from and the date of the regulation, please. She says she hasn't gone back and done a history, we'll have to listen to what it is.

Q This is the 4/1/2006 edition of 201.57?

MR. BARNES: Subsection.

MR. ALTMAN: It's 201.57(e).

MR. BARNES: 4 April 2006.

Q Correct. The labeling shall be revised to include a warning as soon as there is reasonable evidence of an association of a serious hazard with a drug. A causal relationship need not have been proved.

Do you understand what they say here?

A Uh-huh.
Q Is the word statistical association anywhere?
A There's word association, yes.
Q There's not the word statistical association, correct?
A What else is an association?
Q There are -- the FDA has required changes to the warning without any kind of statistical analysis, correct?
MR. BARNES: Objection. If you know.
A I don't know if the changes were devoid of any type of statistical analysis. I can't make that assumption. But that's not what I'm talking about here on page 17 of my report. I'm talking about the fact that Dr. Blume quoted it out of context.
Q Well, Dr. Blume says it is not universally necessary to employ the various methods of epidemiology to establish that there is an association between a drug and a risk?
A How else do you know if there's a statistical association. Association means, statistical association between a drug and a risk if you don't do a study. Whether it be a clinical trial or an observational study. And the CFR doesn't talk

about that. It talks about labeled warnings and clinical versus, i.e. human data, versus animal data. So it makes -- it's a non sequitur as far as I'm concerned.
Q I'm sorry, we're on page 18 that we're now talking about.
A 17, right?
Q No, we're on 18.
MR. BARNES: Why don't -- you jumped from 17 to 18 now. Why don't you direct her where you are.
Q On page 18 there is, it is not universally necessary to employ the various methods of epidemiology to establish whether there is an association between a drug and a risk.
We talked before about companies have changed labels in the absence of any kind of a statistical analysis based upon case reports, correct?
A That is what I address in number -- in page 17.
Q We're not talking about black boxes. We're talking about labels have been changed based upon case reports, correct?
A Labeling has been changed in some cases based on case reports, yes.
Q So when Dr. Blume uses the word association

within a regulatory context as the FDA has it here, it does not necessary imply there's a statistical association required, correct?
A No, that's not correct.
Q So is it your opinion that the FDA requires a statistical association to make a labeling change?
MR. BARNES: How much time do you have?
THE VIDEOGRAPHER: Two minutes.
MR. BARNES: Take a break now.
Q We have a question on the table first so why don't we --
A Repeat the question.
MR. BARNES: Repeat the question. I'm sorry.
Q Okay. So is it your opinion that the FDA requires a statistical association to make a labeling change?
A I already said that there have been labeling changes based on things other than statistical associations.
However, Dr. Blume is saying it's not necessary to use epi to establish whether or not there's an association between a drug and a risk.
I don't know how the heck you can do that without using some type of epidemiologic method, be it

experimental or observational. That's different from a label.
Q Okay.
MR. BARNES: We should probably break.
THE VIDEOGRAPHER: Going off the record. The time is 2:42 p.m. This is the end of tape number 4.
(Off the record.)
THE VIDEOGRAPHER: We're on the record. The time is 2:57 p.m. This is the beginning of tape number 5.
BY MR. ALTMAN:
Q We were talking about the meaning of the word association and one of the things I want to get some clarification on I guess right above the double quotes, the case reports. You have a sentence, to test for an, and in parentheses, statistical association requires statistical test?
A Where are you?
Q I'm on page 18 towards the bottom. Right above the big quote. The sentence right above the big quote.
A To test for statistical association requires a statistical test. Yes.
Q And you were pretty clear -- you didn't

just say to test for a statistical association, you put statistical in parentheses, correct?

A Yes. Because the word association has been thrown out without putting statistical in front of it, I wanted to make that point, yes.

Q You have a citation there from Strom, which is I believe Dr. Brian Strom, correct?

A That is correct.

Q And I guess that's Pharmacoepidemiology, the fourth edition we're probably talking about here, 2005?

A It's in the back. It's the most recent version.

Q The quotation that you put there is: Certainly one cannot usually determine whether the adverse event outcome was due to the drug exposure or would have happened anyway. Did I read that correctly?

A That is correct.

Q What he's saying there is that sometimes you can tell, correct?

MR. BARNES: Objection. Misstates what it says.

A It says, usually that is not the case.

Q That doesn't mean always, correct?

A There are rare, unique circumstances in

your review of materials in this case?

A No, I did not.

Q The bottom paragraph that starts in paragraph 29. I believe it's the fourth line, it says: Because there is no placebo group, there is no basis to evaluate benefits and risks. Did I read that correctly?

A Yes.

Q Are you aware that the FDA will not allow you to use open label uncontrolled studies to demonstrate efficacy but does use uncontrolled studies to evaluate risks?

MR. BARNES: Objection.

A Can you repeat that, please.

Q Are you aware as to whether the FDA will allow you to use uncontrolled studies to evaluate risks?

A It is my understanding that all the clinical data, controlled and uncontrolled, gets put into a safety summary for an NDA. So both -- all clinical data is discussed and looked at for potential events.

Q Well, you say here because there is no placebo group there is no basis to evaluate benefits and risks and we're talking about uncontrolled studies,

which you may be able to link a drug to a disease. They're usually very unique events that are very, very rare, like one in a million, that often they're almost always associated with a drug effect. They have very low background rates. Like Steven Johnson syndrome. But otherwise it's -- we like to find the one unique case, but in the most part he is correct, it is usually not the case.

Q So with all of those your answer is yes, sometimes -- usually does not mean always, correct?

MR. BARNES: Objection. Asked and answered. She's responded. Answer it again.

Q That's okay. I'll move on.

Page 19. Third paragraph you say: Individual case reports involving patients who were dechallenged, parentheses, taken off the medication, closed parentheses, and the reaction resolved and subsequently rechallenged, parentheses, put back on the medication and the reaction occurred, closed parentheses, may in rare circumstances provide evidence of a causal relationship between the drug and an adverse effect. Did I read that correctly?

A Yes.

Q Did you actually review any of the case report forms from any of the clinical trials as part of

correct?

A Right. There is no way to see if there's statistical association between the certain outcome, be it beneficial or harmful and drug exposure.

Q Is it your position the only way to assess whether there's a risk in a drug is through a statistical association?

A That's not what I said. I said there's no way to test for a statistical association if you don't have a comparison group, an unexposed group.

Q Okay. Page 20. Opinion four. Using the published and accepted methods for calculating PRR, there was no signal of disproportional reporting, SDR, for reports of completed suicide with Neurontin until 2005 and suicide attempt until 2006.

Did I read that correctly?

A Yes, that's what I wrote.

Q This is consistent whether compared to a background rate of all drugs or the antiepileptic drugs in the FDA analysis. Did I read that correctly?

A Uh-huh.

Q There was no SDR for suicide attempt when compared to other ADEs to date. Did I read that correctly?

A That's correct.

Q Based on my analysis of the evidence, Pfizer is correct in concluding that it did not see a signal for suicidality with Neurontin in the adverse event reports. Did I read that correctly?
A Yes.
Q Let's take that last sentence there.
MR. BARNES: This is like the first sentence we talked about earlier?
MR. ALTMAN: No. This is a different sentence and a different opinion.
MR. BARNES: Okay. This is separate from the question one, okay.
MR. ALTMAN: This is different opinion.
A Can I clarify --
Q Sure.
A -- that opinion one also?
Q Sure.
A I want to make sure before we go into very similar issue. Where is opinion one. Opinion one I'm addressing FDA meta-analysis which I had said and the FDA meta-analysis does not show a significant association for Neurontin.
So what I'm saying is taking that and all the previous information, which I cover in my first report, there's no basis for saying that there's an

A And also all the other reports and literature, for example, the Patel, I relied on that, EMEA report. There's a number of other reports of clinicians who have evaluated the individual case reports.
Q Well, those were all done in response to the FDA suicide inquiry, correct?
A I'm not sure why they were all done. So I can't make that assumption.
Q Are any of the reports from the Warner-Lambert, Parke-Davis, did you review any documents from Warner-Lambert, Parke-Davis?
A I don't recall who was the author or what period of time at this point. I can't remember. I don't recall.
Q Did you review -- just appearing from your list here I don't see that you reviewed -- strike that.
The response to the EMEA was substantially the same as the response to the FDA, correct?
MR. BARNES: Which one, the Parson's report in '04?
Q We're all talking about reports from '04, '05, '06, correct?
MR. BARNES: That's what I'm making sure.
Q That's what I'm trying to get at. We're

association or signal with Neurontin and suicidality.
So adding, what I'm trying to explain is adding the FDA meta-analysis does not give you anything new. So I want to clarify that because it also relates to this.
Q I still want to clarify, though, that your statement as to signal is related to data mining, correct?
A In which one?
Q Either one.
A There's is nothing in data mining, there's nothing in the meta-analysis. I can't find any in the clinical trials. I can't find anything in the epi-literature that would suggest that there's a signal. There's definitely no statistical associations.
Q But you didn't review the case report forms from the clinical trials, correct?
A No, but I understand they were reviewed by experts and then submitted to the FDA for their meta-analysis.
Q But once again, though, what I'm getting at is you did not -- your statement, though, is limited to a data mine review of the spontaneous adverse event reports of an FDA meta-analysis, correct?

not talking about some analysis that was done before the FDA first called Pfizer, correct?
A Well, we're talking about adverse event reports that were coming in since the beginning of the drug approval, so.
Q I understand but did you read --
A They're summarizing all the data from day one.
Q Did you read any -- what I'm interested in, did you read any particular document that shows the company had reviewed suicidality overall in a time period before the FDA first called them in the beginning of 2004?
A In 2004. I'd have to go back. I don't recall.
MR. BARNES: Certainly to the extent that she relied on or considered it would be in her references reviewed. Certainly 2004, 2005, 2006 time period she has cited those and discussed them at length in her first report.
Q I mean, frankly, what I'm trying to get at is if there was something in let's say 1995 or 1996 timeframe that was not related to a data mining evaluation that suggested there was a problem, you didn't review any of that information, correct?

A I didn't see anything.
Q Did you look?
A Did I look? Did I go through boxes of company documents? No, I did not go through boxes of company documents. I don't recall seeing any information at all.
Q And you also, I think, said in the -- outside of the context of a data mining finding or a statistical meta-analysis and things like that you're not qualified to review the clinical information to see if there's something there suggestive that there's a problem, correct?
A I can review the epidemiology and tell you about the study. I can look at the data mining, but I am not a clinician.
(Conference call interruption.)
Q So, for example, if there was a case series in 1994 or 1995 that suggested there could be a problem, you didn't review a case series to see if there was really a problem there, correct?
MR. BARNES: Objection. Assumes facts not in evidence. You may answer.
A If hypothetically there were such a series, I would not be evaluating it.
Q Okay.

Did I read that correctly?
A Yes.
Q You cite there to a document Woodcock J. 2002, correct?
A Yeah, Janet Woodcock gave the talk about the periodic.
Q Once again, the way you've done it here is would a reasonable reader conclude that the FDA sentence comes from Janet Woodcock's report?
A I didn't put quotes on it.
Q But the concept of that, you're citing to something, you're attributing that to something. What part of what I just read are you attributing to Janet Woodcock?
A That they stopped entering manufacturer's periodic reports.
Q Well, you say nonserious adverse event reports?
A Yes. The nonserious periodic. It's very unclear from the FDA if there's any rhyme or reason to what they do and don't when they started AERS.
Q I'm going to mark the next exhibit which I believe is 23.
(Whereupon, a document was marked as Deposition Exhibit Number 23.)

A Clinically, that's not my expertise.
Q And that's why I'm just trying to understand. When you say there was no signal, you're basing that just upon the adverse event, a data mining finding or the meta-analysis kind of thing?
MR. BARNES: Or the 2004, 2005, 2006 reports to the FDA.
Q Correct.
A I'm basing it on my review of all the information that I reviewed from the reports of the safety summary, my evaluation of the AERS data, the epidemiological literature, the FDA meta-analysis. There's quite a lot of documents I reviewed. So all of these.
Q Okay. That's fine.
The first paragraph there?
MR. BARNES: Page 18 again?
Q No, we're on page 20. First full paragraph. You make the statement: These include, but not limited to, a change in the dictionaries used to code adverse events from COSTART to MedDra, a lifting of limits on the number of adverse event terms that could be listed on each adverse event report, and not entering periodic manufacturers nonserious adverse event reports into the database.

MR. ALTMAN: It's really not necessary to read the whole thing.
MR. BARNES: Well, if she feels like she needs to read it, she can read it.
MR. ALTMAN: I just want to point her to one particular paragraph which is where her citation comes from.
MR. BARNES: I'm not sure she's cited a precise page.
BY MR. ALTMAN:
Q Well, could you please go to page five of nine. Do you see where it says adverse event reports?
A Hang on. I'm getting there. Okay.
Q She talks about the adverse event reporting system, correct?
A Yes.
Q There's the sentence about five lines down that says presently, do you see that?
A Yes.
Q It says: Presently all manufacturer reports of serious events and all direct reports are entered into AERS database. Did I read that correctly?
A Yes.
Q It says: Nonserious manufacturer reports are not usually entered into AERS. Did I read that

correctly?
A Yes.
Q Is that the same as saying they're not entered into AERS?
A I could have been a tad more precise. I have been trying for quite awhile now to see if there's any specific, what do you call it, system that they've set up on what gets entered and what doesn't get entered.
It appears to me that they just stopped with AERS entering reports because they just didn't have the resources. So it's not clear what they're entering and what they're not. But they are not entering usually, so I'm not quite sure usually means, they're not entering every periodic manufacturer's report.
Q Did you ever run an inquiry through Q Scan on your own to see if there are any periodic nonserious reports in the FDA database?
A There are.
Q If I told you that there were several hundred thousand periodic nonserious adverse event reports, do you have any basis to dispute that?
A Under what time period?
Q In the AERS era?

A In the AERS --
Q AERS.
A -- there are.
Q -- several hundred thousand?
A There are, exactly. So it's not that they don't enter -- they enter some of them. They don't enter all of them.
In fact, it's changed where the periodic reports used to be the majority of reports and now there are significantly less periodic reports than there are expedited reports.
It's actually shifted. I don't mean to say that they don't enter any individual periodic reports. But they don't enter all of them.
Q That's a reasonable interpretation what you wrote in your expert report, correct?
MR. BARNES: What is a reasonable interpretation?
Q That they don't, when you say and not entering periodic manufacturer's nonserious adverse event reports into the database. Somebody reading that would take that they don't enter nonserious reports in the database, correct?
MR. BARNES: Objection. Calls for speculation. It's a state of mind of others.

Q Is that a reasonable interpretation --
A No.
Q -- of that sentence?
A That's not what I meant. I could have been more explicit. But no, I did not say they don't enter any.
Q Would somebody reading this know that you didn't mean that they don't enter any?
MR. BARNES: Same objection as to the state of mind.
A I don't know. I don't know what someone would interpret.
Q But we can agree that the nonserious reports that are in there -- it's not consistent as to when they go in? You said yourself you haven't been able to find the pattern of when they go in and when they don't go in?
A I know they stopped entering them and then they started encouraging companies to ask for waivers for having to report individual reports. So many companies now have waivers by NDA to not have to give individual reports. They just give periodic safety summaries of the reports.
Now, the FDA might also get reports from companies that don't have waivers and choose not to

enter it. It doesn't seem to be a hard fast rule. I believe they tried to enter the ones for newer drugs and leave the ones for the older drugs. It's been prioritized. But, again, there is no published hard and fast rule of what they're entering and what they're not entering.
Q So if one was going to do an analysis of -- that could involve proportional reporting, could it substantially bias the analysis by including nonserious reports when it's completely unclear as to some companies send in nonserious reports, some companies don't send in nonserious reports that may come from different sources?
A There are so many sources of bias in evaluating AERS data and that may be, depending on what the outcome is that you're looking at.
MR. ALTMAN: Objection. Nonresponsive.
Q I'm asking going to ask you very specifically.
If some companies send in nonserious reports and some companies don't -- if one company sends in nonserious reports and another company didn't send in the nonserious reports, and you calculated the percentage of -- of a particular adverse event over the total number of reports, that could substantially bias

those findings if companies had differential reporting, correct?

A What you are doing with the percentages, I think that's going to depend on whether or not you're going to see a bias.

Q If you're comparing the percentage of a certain adverse event report from one drug to that of another drug and one manufacturer submits nonserious reports and the other one does not submit nonserious reports, can that alter what you see?

A Depending on many issues, including what is the event that you're looking at. So if you're looking at a serious event this may be moot.

Q But if you're comparing the total number of adverse events, won't you have more potentially more adverse events for one, including all the nonserious reports than for the other?

A There's many more things that impact reporting and reporting rates that can give you bias. Including how long the drug has been on the market, for example. Whether there's notoriety bias. How the drug is used, the population, the sales. So there's so many issues. Anything can bias. I don't say anything, but there's so many things that can bias the numbers.

MR. ALTMAN: Objection. Nonresponsive.

would be comparing apples and oranges.

Q It's the same -- I'm sorry.

MR. BARNES: Go ahead. I have an objection. The objection is, are you stating that there are -- there were nonserious reports of suicide which by definition is death?

Q No. Total number of reports for that particular drug there's a thousand of them, of which 900 of them are nonserious and 100 of them are serious because they send in nonserious reports. If you don't take the serious and nonserious issue into account, what percentage of the reports, 10 out of a thousand, do you get?

MR. BARNES: Objection. Assumes facts not in evidence. Incomplete hypothetical.

A But the thing is it doesn't make sense because you haven't told me anything else. What about direct reports. You're going to get serious and nonserious direct reports.

Q There's a total of a thousand reports for that particular drug, 100 of which are serious and 900 are nonserious. If you have 10 suicides and you look at the total number of reports, what percentage of the reports is 10 over a thousand?

A 10 over a thousand, very specifically, is

Q Let's do a concrete example.

Drug A has 10 reports of suicide out of 100, serious reports. Drug B has 10 reports out of -- of suicide out of a thousand reports?

MR. BARNES: Serious reports.

Q Of which 900 of them are nonserious. What's the percentage for the first drug, 10 out of 100, what's that percentage?

MR. BARNES: Objection. Assumes facts not in evidence. Incomplete hypothetical. If you can answer that, go ahead.

A You're losing me here.

Q If 10 out of 100 serious reports are suicide for one drug, what's that percentage of reports that are suicide?

A 10 divided by -- what did you say 100?

Q 100.

A So you're talking about 10 percent of the reports.

Q Now, if another drug has a thousand -- 10 suicides also but has a thousand reports of which 900 of them are nonserious, but you don't take that into account, what percentage is 10 out of a thousand?

MR. BARNES: Objection to the --

A That doesn't make sense because then I

one percent.

Q Now, if you only looked at serious reports it's 10 over 100, what percentage is that?

A I can tell you the percentage, the number, you mean just do 10. 10 out of 100 is 10 percent.

Q So if I compare drug A, which was 10 percent, to drug B when I don't take -- when I leave the nonserious reports in, it looks like drug A has 10 percent of its reports are suicide and drug B has 1 percent of its reports are suicide, correct?

A Wait a second. This is very hypothetical. I can tell you 10 divided by is 100 is 10 percent. One divided by a thousand -- 10 divided by a thousand is 1 percent.

I'm not comparing drugs. You're comparing drugs. I wouldn't just do that. That's why I have to say that's why I did my PRR for the entire background because I don't -- then you have it all averaged out across all the drugs. So that gives you the more stability.

That's why you don't necessarily present this proportion and this proportion. You do proportional reporting rate. So you know your numbers are off. You hope that you have bias is random bias. And therefore you divide and you have a stable estimate

of the effect. That's why you don't present proportions.

MR. ALTMAN: Objection. Nonresponsive.

I'll ask it a different way.

Q If a drug has a thousand adverse event reports, 900 of which are nonserious and 100 of which are serious and has 10 suicides, overall what percentage of the adverse event reports is that 10 out of a thousand?

A 10 out of a thousand is 1 percent.

Q If you only look at the serious reports of 10 out of 100, what percentage of that?

A 10 out of 100 is 10 percent.

Q There's a difference between those two things whether you look at the nonserious reports or not, correct?

A This is all very hypothetical --

Q If you include the nonserious reports, does that change the percentage?

MR. BARNES: Objection. Completely hypothetical. Go ahead.

A It's so hypothetical. I mean, the context of which you're comparing two drugs is really, really -- I wouldn't just say oh, I'm going to compare these two drugs. It's -- there's so many other factors

that need to be taken into consideration and I would be really suspect to compare two drugs. Were they approved in the same time period, are they used for the same use, do they have the same indications, do they have the same type of populations using the drugs. There's so many issues.

MR. ALTMAN: Objection. Nonresponsive.

Q If you include the nonserious reports for that particular drug, does it change the percentage?

A If you include --

Q If you find the percentage of all reports, including the nonserious reports, do you get a different percentage and if you only get the percentage just using the serious reports?

A How can you use the serious reports if they're not in the -- the nonserious reports if they're not available.

Q I'm not asking, this hasn't got anything to do with the FDA. I'm just telling you for a given drug, there's a thousand reports, 900 -- let's try it one more time.

Drug has 900 nonserious reports and 100 serious reports and 10 suicides. If you take the percentage of all reports, what percentage do you get?

A We just said that, 10 divided by a

thousand.

Q Is?

A Is -- now I'm getting tired, 1 percent.

Q If we only use the serious reports, we have 10 over 100, correct?

A Wonderful.

Q What percentage is that?

A That's 10 percent.

Q And 10 percent is different than 1 percent, correct?

A I would agree with you there. 10 percent is not 1 percent.

Q So including the nonserious reports in your calculation changes the percentage, correct?

A I would assume that all suicides are serious.

Q But if you calculate --

MR. BARNES: Let her finish her answer. Go ahead.

A That's all. All suicides are serious.

Q We're not talking about the numerator, we're talking about the denominator.

A If you change your denominator, your numbers will change, that is correct.

Q So if you don't use the nonserious reports

you get a different percentage than if you use the nonserious reports, correct?

A If you use them and if you don't use them. They're either there or they're not there.

Q Well, suicide is serious?

A Absolutely.

Q Getting rid of the nonserious reports is not going to change your numerator, correct?

A I don't believe it would.

Q So you're going to get a difference whether you include the nonserious reports or not?

A If you change your denominator you'll get a different number.

Q Now, if you're comparing groupings of drugs, if you want, not individual drugs. If your denominator sometimes contains nonserious reports and sometimes does -- sometimes contains nonserious reports and sometimes doesn't contain nonserious reports, can that bias your comparisons between the two because of that?

MR. BARNES: Objection. Vague.

Q Purely because of the existence of nonserious reports in the database?

MR. BARNES: Objection.

Q I'm not talking about any other biases?

MR. BARNES: Objection. Vague. If you can answer that, go ahead.
A I'm not sure I can. There's just so many things that are happening in the data and this is just one of many, many things in the data that can, you know, anything can change the numbers. That's why it's called data mining.
Q Okay. Do you have any evidence that Pfizer, Parke-Davis or Warner-Lambert before Pfizer, purchased or did any kind of data mining?
A I haven't reviewed any of their SOPs. I'm not quite sure what they did.
Q Aside from SOPs, did you see any evidence in any documents that they did any data mining?
MR. BARNES: Vague as to data mining. This is using mining a FDA database or their own database.
Q Data mining. We have been talking about data mining all day.
A The only one I'm aware of is I know Manfred Hauben is very well-respected in the field of data mining. He's published extensively and he works for Pfizer so, therefore, I would assume --
MR. BARNES: Don't assume.
A -- that he does data mining, but I don't know within any one drug what they do. I'm not privy

an e-mail dated March 15th, 2001 from Lester Reich to Manfred Hauben.
Q You're obviously taking some time to review it. Why don't you go ahead and do that.
(Witness reading.)
A Okay.
Q Have you had a chance to review this document?
A Sure.
Q Have you ever seen this document before?
A No, I haven't.
Q Do you know whether any of the other experts in this case were provided with this document?
A I don't know.
Q Would you please read in -- I'd like you to read for the record the first sentence under objective.
A With the post marketing use of Gabapentin in patients other than with epilepsy it is important to identify whether these new populations may be particularly susceptible to specific adverse drug effects both labeled and unlabeled and to identify conditions under which specific adverse events may be more likely to occur in these new patient populations.
Q Do you agree with that statement?
A Yes.

to their protocol.
Q Did you see any documents that suggested Pfizer had done any data mining?
A In this case, no, I have not.
Q I'm going to mark Exhibit No. 24.
(Whereupon, a document was marked as Deposition Exhibit Number 24.)
MR. BARNES: Counsel, if you could, this is an incomplete document. Do you have the full document for us to review?
MR. ALTMAN: This is a complete document, I believe.
MR. BARNES: Are you sure?
MR. ALTMAN: I'm pretty sure it is. It's a document marked Manfred. It's a three-page document marked Pfizer, underscore, MHauben, H-A-U-B-E-N, underscore 0000123.
MR. BARNES: Do you have a date on this document? It's a document without a date.
MR. ALTMAN: I can probably look to the document before.
MR. BARNES: I think it's probably a document that comes with other documents. It should give us a reference to a date and time.
MR. ALTMAN: It appears to be attached to

Q Were you aware that at this time the company was in the process of seeking approval for its neuropathic pain indication?
A I don't have any date on this. I don't know what the time period is.
Q It's March of 2001?
MR. BARNES: What's your question again, Counselor?
Q Were you aware that at this time the company was in the process of seeking approval for its neuropathic pain indication.
A I wasn't involved in this in 2001.
MR. BARNES: No, the question is: Were you aware that at this time the company was seeking approval for a neuropathic pain evaluation. If you're aware.
A No, not necessarily, no.
Q Why don't you go down, skip the next sentence. Why don't you read the next -- well, you know what, read the next sentence. Why don't we read the next two sentences, that will take care of it starting with the development.
A The development of the safety profile of any drug product is an evolving process.
Q Do you agree with that sentence?

A Sure.
Q Read the next sentence.
A As with any marketed drug in order to provide guidance for the safe and judicious use of Gabapentin for the specific clinical application which we are seeking in the United States, neuropathic pain, accumulation and analysis of the broader population's safety experience is critical for the ongoing development of an accurate safety profile.
Q Why don't you read the next sentence.
A The intent of this review is to summarize the experience of the overall population using the ICH pharmacovigilance safety update report format with additional focused reviews of selected events for potential signals which might be of particular relevance to the neuropathic pain population.
Q Does this document stand for the proposition that there may be adverse events that will affect certain populations differently than other populations?
MR. BARNES: Objection. If you know.
A I don't see that in what I read.
Q Were they expressing a concern that maybe there are signals that may be particular to a certain population using their drug?

A Say that again, please.
Q Does this document suggest that they wanted to review to see if there were potential signals which might be of particular relevance to the neuropathic pain population?
MR. BARNES: Take your time and read it.
A Not necessarily. They're looking for, as they say here, potential signals that might be of particular relevance to the neuropathic pain population.
Q The first sentence, these new populations may be particularly susceptible to specific adverse drug effects?
A Where are you?
Q The first sentence, about the middle of the second line.
A Okay, I see that.
Q So they were looking at potentially seeing whether Neurontin could affect the neuropathic pain population differently than the epilepsy population, correct?
MR. BARNES: Objection. Document speaks for itself.
A Yeah, I can't speculate beyond what's written here. This is the first time I've seen it and

it's not with much context.
Q Go to the second page, please. I'd like you to -- you see where it says psychiatric, nervous system?
A Yes.
Q Under section 5. It says: Review of events of relevance to the neuropathic pain population. Did I read that correctly?
A Excuse me?
Q It says: Review of events of relevance to the neuropathic pain population. Did I read that correctly?
A Under E, section 5, yes.
Q The intent would be to note whether there were possible signals of specific adverse events in the neuropathic pain population that may be diluted by the overall population to assess the strength of any signal. Did I read that correctly?
A Yes.
Q The last sentence: The intent of the review of these events is to satisfy ourselves that the neuropathic pain population is not at an increased risk to develop these specific events. Did I read that correctly?
A Uh-huh.

Q Then underneath that it says: Psychiatric and parentheses nervous system, correct?
A Okay.
Q It says: Patients with chronic neuropathic pain may represent a population with significant amount of co-morbid depression, in parentheses 150 cases, and suicide 15. Therefore these cases will be looked at to include or exclude any significant signal of drug induced depression/worsening. Did I read it correctly?
MR. BARNES: Well. You didn't read it correctly. You said 15 cases after suicide and it just says paren 15.
THE WITNESS: 15, yeah, that's true.
MR. ALTMAN: I stand corrected.
MR. BARNES: Well, I mean.
MR. ALTMAN: I understand. That's fine.
A Depression, slash, worsening.
Q Depression, okay.
Does this suggest that they felt that there could be -- they wanted to investigate whether there was a difference in the neuropathic pain population with respect to depression?
MR. BARNES: Objection. Document speaks for itself. You can answer if you know.
A It doesn't say that.

Q They wanted to review events of relevance to the neuropathic pain population, correct?
A That's correct.
Q This is part of that section for which I just reread the first sentence, correct?
A This is a section under section 5, yes.
Q Okay.
A But it doesn't appear that they're comparing it to anything. They're just looking between the population.
Q I didn't say they were comparing it. I just said they wanted to see if there were any potential signals, correct?
A Can we read what you said.
Q I'll read: The intent would be to note whether there are possible signals of specific adverse events in the neuropathic pain population. Did I read that correctly?
A That might be diluted by the overall population.
Q And to assess the strength of any signal. Did I read that correctly?
A That is correct.
Q Do you know what they were going to compare it to to do that?

MR. BARNES: Objection. Assumes facts not in evidence.
A It doesn't say.
Q It doesn't say. So it's not clear that they were going to compare that to anything, is it?
A I can't make guesses on what they were going to do and not do.
Q Okay. Would you agree with the following: Do you agree or disagree with that section on the psychiatric as started with patients with chronic neuropathic pain that I read before?
MR. BARNES: I'm not sure I follow.
Q Do you agree with the statement, patients with chronic neuropathic pain may represent a population with a significant amount of co-morbid depression and suicide. Did I read that correctly?
A That's what the document says.
Q Do you agree with that sentence?
A From the readings that I've done that is what I have seen in the literature, yes.
Q Would you agree with the following sentence: Patients with bi-polar disorder may represent a population with a significant amount of co-morbid depression and suicide?
A Where is this?

Q I'm just asking if you agree with that sentence?
MR. BARNES: Are you representing to her that it's in this document or is it a new question?
Q It's a new question. It's not in the document?
A Oh.
MR. BARNES: It's late in the day. If you're switching back and forth you should tell her. Go ahead. She was looking for the sentence.
Q Sorry. Do you agree patients with bi-polar disorder may represent a population with a significant amount of co-morbid depression and suicide?
A That is what I understand from the literature that I reviewed.
Q Does the document suggest that they were going to look at psychiatric -- reports of depression and suicide in the neuropathic pain population to see if there was a signal?
MR. BARNES: Objection. If you know. Suggest to her?
Q Does it suggest to you that that's what they were going to do?
A It says are very specifically cases will be looked at to include or exclude any significant signal

of drug induced depression or worsening depression.
Q Nowhere in what we read here did they talk about doing any kind of data mining along those lines, correct?
MR. BARNES: In 2001, right?
Q In this document do they discuss data mining?
A They don't discuss what type of analysis they're using in this document.
Q But if they were going to review -- but they talk about reviewing individual case reports, correct?
MR. BARNES: Do you want to point her out so you can find it.
A Where are you talking about?
Q Same sentence we just read under psychiatric. It says: Therefore these cases will be looked at to include or exclude. Does that suggest they're looking at cases?
A I assume so. I'm not quite sure what they're doing.
Q Did you see any evidence that they ever did an analysis of psychiatric adverse events associated with the neuropathic pain population?
MR. BARNES: Objection. Lack of

foundation. Lack of predicate. You might want to ask her if she looked to determine this. I think she told you she has not looked at these materials in her report.

Q I'm not asking if it's material. I'm asking did you see any evidence that Pfizer -- in the period before the suicidality review in 2004 -- that Pfizer or Warner-Lambert or Parke-Davis ever conducted such an analysis?

MR. BARNES: Prior to 2004?

Q Prior to 2004.

A That was not part of the data that I reviewed.

Q Do you see anything in here, going back to page one of this document under overall description of post-marketing data set. Section one. Total number of cases and events. Is that really a data mining chart that they were going to create or is that more just simple counts of adverse events?

MR. BARNES: If you know.

A I don't really know what this is. This is the first time I've seen it and it's with very little context. So I'm not quite sure what this is and what it means. Beyond telling you what it says again, that's about all I can say.

this before that lists adverse events?

A There were appendices in one of the reports that had similar listings, yes.

Q You've seen that in this case and what about outside of the context of this case. Have you ever seen a listing of adverse events similar to that particular report we just looked at?

A I may have. I'm not a clinician so I don't review that type of data.

Q Have you ever prepared one?

A No, I haven't.

Q Do you think it takes a clinician to prepare a line listing like that from the adverse event database?

MR. BARNES: What do you mean by prepare?

Q To write a report of the adverse events in the adverse event database?

A I think it takes a clinician to select the relevant terms to --

Q But if I --

A -- study.

Q I'm sorry. But if I gave you a list of terms and said please provide me a listing of all the adverse events in this period of time with these terms, does that require a clinician to do that?

Q Does this suggest that they were going to produce some kind of a line listing?

A I don't know what they were going to do. I could only tell you what it says.

Q If the company was -- if the intention here was that the company was going to do a line listing, do you think there was anything -- is that a -- do you know what a line listing is in terms of adverse events?

A Within -- maybe you better define the context you're using it in.

Q In the context of adverse events, have you ever seen a line listing that's similar to what we looked at earlier, that one chart of that listing of adverse events. You know, it had the adverse event number and the date and the age and what the events were, et cetera. You've seen those before, correct?

MR. BARNES: Objection. Vague as to line listing.

A I've seen MedWatch reports.

Q It's not a MedWatch report. Have you ever seen a document -- that right there.

MR. BARNES: Are you representing this is known in the industry as a line listing, I wouldn't accept that.

Q Have you ever seen a document similar to

A To just pull data?

Q Yes.

A Probably not.

Q Is that something you've ever done before in the past?

A Yes, I have.

Q Can you remember the first time you did something like that, approximately? Did you do that in the early 1990s?

A (No answer.)

Q I'll ask the question a different way. Was there any new found technology that didn't exist in the early 1990s that would have prevented somebody from creating a line listing like that, to your knowledge?

A Only that the technology was slow when things took a lot longer, more difficult to work with larger databases in the 90's. Absolutely.

Q But aside from that, they could have generated a volume listing like that in the early 1990s, correct?

A I don't know what systems were in place in the 1990s. I'm not familiar with them.

Q Suffice as to say, you didn't see any evidence that the company ever did an analysis similar to Exhibit 24 for any off-label indication, correct?

MR. BARNES: Objection. Asked and answered.
Q By off-label indication?
MR. BARNES: I think she said --
A I didn't look for any.
MR. BARNES: She didn't look for it and she has put in her materials considered. You've ask for that three different ways. She doesn't know what they did.
Q Well, you haven't seen it in any document -- not the document itself, but you didn't see a reference to it in some document, correct?
MR. BARNES: That was also before the Parson's report in 2004.
MR. ALTMAN: Before the Parson's report.
MR. BARNES: So before the Parson's report and after March 2001 did you see anything in regard to analysis that was based on the report like this?
Q At any time before the Parson's report.
A Just the summary of the data that was in the Parson's report. I didn't ask for anything and I didn't get anything.
Q Did you see any evidence in the Parson's report that they referred to that they had done a similar analysis at an earlier point in time?

MR. BARNES: Objection.
Q -- comparing individual drugs?
MR. BARNES: Objection. Assumes facts not in evidence. You may answer.
A It is my understanding from what I read from Dr. Blume's report that she never did any disproportional reporting analysis.
Q But she calculated percentages of adverse event reports, correct?
A She calculated percentages of higher level term over reports for a number of different drugs. That's what -- I have to look at the original report.
Q That's fine. You said that it was inappropriate to do that and I think that you should do this against the background of all drugs, correct? And you actually did that in your original report, correct?
MR. BARNES: Is your question that a PRR should be prepared the drug of interest against the background of all drugs in the database. Is that your question? It was unclear.
Q Yes, that's what I think you said in your original report.
A Could you please show me where you're talking about?
Q Okay. Let's do this a little differently.

A I believe the Parson's report referred to their safety summaries that had been done and reported to the FDA.
Q Talking about part of the FDA, correct?
A As part of the legal requirements of having a marketed drug, yes.
Q You were, in your original report, you were critical of Dr. Blume for having compared individual drugs and complained, for lack of a better term, that she had said this was actually a proportional reporting rate analysis when it was not. Do you recall that?
A Which page are you on?
Q Just generally. This happened in the deposition we discussed this. It's a general proposition.
A It's a big report. There's quite a few pages. What specifically are you talking about?
Q Let's do this a little different.
In your original report you did a PRR analysis of Neurontin against all drugs, correct?
A I calculated the PRR for suicide and suicide attempt with Neurontin compared to the rest of the FDA data.
Q Do you recall that Dr. Blume did a disproportionality analysis --

When you did your original report, you calculated the PRR of Neurontin against all drugs other than Neurontin in the database, correct?
A In the FOI AERS database for those two events that I mentioned.
Q Why did you use the background of all drugs?
A Because for a basic signal detection that's what I typically use in my practice, yes.
Q Okay. And you -- but this time you did it against a subset of drugs, correct?
A I did.
Q So it's not inappropriate to use a subset of drugs when you do comparisons, correct?
MR. BARNES: Objection. Vague.
A In data mining it would not necessarily be inappropriate. Depends on your protocol and what you're doing. But you need to have an appropriate comparison calculated test statistic. I think that's an important difference of what I did and what Dr. Blume did. One of the many differences.
Q I'm going to mark as Exhibit 25.
(Whereupon, a document was marked as Deposition Exhibit Number 25.)
Q This is a chart entitled: Cumulative

Percentage Reports of Suicidal and Self-Injurious Behavior for Neurontin versus Background of All Other Drugs. Did I read that correctly?

A Okay.

Q This is a chart that was contained in Dr. Blume's report, correct?

MR. BARNES: The report or her declaration?

Q I'm sorry. Her declaration.

A I believe so, I believe so.

Q Now, I'd like you to look at the first quarter of 2000. Can you see that? It's about two dots to the right of the arrow on the -- do you see where I'm talking about?

MR. BARNES: I can't tell.

Q Two dots to the right of the arrow.

A When it hits 3 percent?

Q Correct.

A Okay.

Q Can you read what the background is approximately there?

A What is the background here?

Q Background is all other drugs, other than Neurontin. At that point in time what's the percentage of the background of all other drugs approximately?

A Oh, I don't know, just over 1 percent.

Q And it's your position that you can't tell what the ratio is by looking at these two lines?

A I didn't say that.

Q If this was .03 percent and .01 percent, what would the ratio be?

A It would be the same.

Q That might mean something different to somebody who is reading this chart than 3 percent and 1 percent, right?

A Potentially.

Q Something that occurs at .03 percent of the reports versus 3 percent of the reports is quite a bit of a difference, isn't it?

A That's a whole different issue, irrelevant absolute differences.

Q So in providing the percentages and allowing the reader to do the ratio if they choose to, there's actually more information here than simply providing the ratio of 3, correct?

A It depends on what you're doing.

Q To be able to put what that ratio means in context, the magnitude of the reports giving you the percentages gives you more information than simply the ratio, correct?

MR. BARNES: Objection.

Somewhere.

Q Are you able to calculate what the ratio between those two things are based on what you see here?

A Can I calculate a ratio?

Q Yes.

A Yes.

Q What's that ratio?

A 3 divided by 1 would be 3.

Q So your criticism of Dr. Blume is that she says 3 percent and 1 percent, it doesn't simply say 3; is that correct?

A I'm critical in other parts where I said she says she calculates a PRR and then doesn't.

Q So it's only -- so it's only the labeling issue. It's not as if you cannot figure out what the PRR is; is that correct?

A No, I have a lot of criticisms besides that. That's just one of the many criticisms I have of the work she put forth.

Q That's fine.

A I just want to understand. One of the many criticisms, many of her charts were mislabeled and she purports to do a PRR or at least some measure of disproportionality and doesn't and that's just wrong.

A It gives you different information.

Q Well, it gives you the ratio as well, doesn't it?

A You have to calculate it. It's not there.

Q Okay. But on -- is that difficult to do?

A It would be nice to have the numbers.

Q But is that difficult to do?

A Maybe. Maybe not.

Q As you look at this chart right now at any particular point in time, would you have any particular difficulty in calculating what the ratio is at that particular point in time?

A I could estimate it.

Q You could estimate it pretty closely, couldn't you?

A Depends. Some of them are a little hard to divide than others, but yes, I can estimate the ratio.

MR. ALTMAN: Why don't we take a break.

THE VIDEOGRAPHER: Going off the record. The time is 3:57 p.m. This is the end of tape number 5.

(Off the record.)

THE VIDEOGRAPHER: We're on the record. The time is 4:16 p.m. This is the beginning of tape number 6.

BY MR. ALTMAN:
Q Dr. Weiss Smith, looking at Exhibit 25. Have you done anything to verify whether any of these percentages are correct or not?
A Did I verify these percentages? No.
Q Do you have any evidence that they're not correct, that the data is not correct?
MR. BARNES: As applied or as plotted?
Q As plotted.
A The underlying data?
Q Yes.
A I did not verify yes or no.
Q Does this chart, as it stands, show an alert?
A This chart as it stands.
Q As it stands, as it is right here, show an alert?
A As we define an alert, absolutely not.
Q What's the basis for saying it's not an alert?
MR. BARNES: If you need to read the report, you can.
A One, you need to do data mining, signal of disproportional reporting, you actually have to establish what algorithm and what threshold a priori is

going to be, meaning be called statistically significant. Because there is no standard, you actually have to establish it ahead of time.
Q What threshold do you use for -- take a step back. Basic proportional reporting rate computations effectively take 1 percentage divide it by another percentage or one fraction divided by another fraction, correct?
MR. BARNES: Objection.
A Which statistic are you talking about?
Q PRRs basically compare the fraction of the event over the total -- of a particular event over the total number of reports of that drug divided by the same thing for some background which you define, correct?
A That is the basic calculation for a PRR.
Q Okay. What is the common -- is there a commonly used threshold for a signal used in the context of PRRs?
MR. BARNES: Signal or alert?
Q Alert, sorry. Alert.
A There are actually quite a wide variety in the literature. We have just -- we have a paper under review looking at that. We looked at the literature in the different kinds.

So for all the different data mining algorithm there's quite a range for what people have defined. But the key is you must define it up front before you do the analysis.
Q Is a ratio of two with a chi-square of four and more than three reports frequently used as a threshold with respect to PRR?
A I don't know the frequency of use. It is often available and published in the literature that that is one of the thresholds that people use. So I have seen it published.
Q What other thresholds have you seen people use for PRRs?
A PRR greater than 2, PRR greater than 1.5, with and without N, with and without chi-squared, chi-square greater than 3 --
THE COURT REPORTER: Slow down a little bit.
A Okay. I have a whole paper. But a number of variations of the test statistic, the chi-squared, variations in the number of case reports between one and four. I've also seen people look at confidence intervals. So quite a variety.
Q With respect to ratio chi-square and N, have you seen people use a ratio greater than 2?

A Yes.
Q Is it often that people use a ratio greater than 2?
A I don't have an idea of how often people use it. I could only tell you whether or not we have seen it in publication. Because no one really knows what people are actually using.
Q In reviewing the data that you reviewed for your publication, did you see anybody using a chi-square greater than 2 as a threshold, a ratio greater than 2 as a threshold?
A I believe we did have somebody but I'd have to go back to the paper and look.
Q How many different people did you -- how many different cites did you review as part of your paper?
A Oh, about, we reviewed over 100, but not all of them are accepted and based on our inclusion and exclusive criteria.
Q So of the 100 you saw one that you used a ratio greater than 2, correct?
MR. BARNES: Objection. Misstates her testimony.
A You have to be very careful about the difference between how many times it was published and

how often it's used. So you have a group that's very prolific publication, you could see something published many, many times. And it didn't get the false impression that it's used. But I just want to clarify that. That's very important.

Q But is it frequent that a ratio greater than 2 is used?

A I don't know the frequency of which anyone uses anything.

Q Within your study was it frequent that a ratio greater than 2 was used?

A A ratio of PRR greater than 2 and/or greater than equal to 2 were published quite often in the literature.

Q Greater than -- the ratio greater than 2?

A PRR greater than 2 --

Q Was the threshold --

MR. BARNES: Whoa, whoa, let her finish. Go ahead.

A Or PRR greater than or equal to 2 were often published in the literature as thresholds with or without the N's and chi-squared.

Q Did you see anybody in your study use a chi-square greater than 4?

A That I don't remember.

Q Did you see anybody using an N and greater than 4?

A There were some cases that said N greater than or equal to 4.

Q Greater than or equal to 4?

A Yes.

Q Did anybody say greater than 4?

A I don't recall that.

Q At the third quarter of 2003 in this chart what's the approximate percentage for Neurontin?

MR. BARNES: Third quarter of?

Q 2003. I'm sorry, third quarter of 1999. With the arrow pointed right to it.

MR. BARNES: Do you want to suggest, Mr. Altman, what you think that rate is, since the left axis is --

Q Is that approximately 2.5?

MR. BARNES: Or less.

A Looks a little less than that.

Q 2.4, 2.5, somewhere there. Greater than 2?

A Greater than 2 percent.

Q 2 percent.

A As opposed to a PRR.

Q I'm not talking PRR. Greater than 2 percent. About 2.4 percent?

A Yes, it's greater than 2 percent.

Q And the background, is it about 1 or 1.1 percent?

A It's about 1.1 percent. Of serious suspect reports with HLT of Neurontin.

Q That's correct. I understand.

What is that ratio at that particular point in time, is it greater than 2?

A The ratio would be just barely above 2. Somewhere around there.

Q And you see the chi-square there is 6.7, correct?

A So help me here. Where did you -- do you have a chi-squared for each data point?

Q There's a chi-square for that data point. The chi-square there is 6.7?

A And that is comparing what, because there was no protocol --

Q Comparing those two percentages?

A Comparing these two percentages for the HLT.

Q For this chart as it is, the chi-squared is 6.7? Do you see that on the chart?

A I see that.

Q Do you have any basis for saying it's not

6.7?

A I didn't redo your analysis. I don't do an analysis like this. I don't think this is an appropriate analysis.

Q Is that because it doesn't show the actual ratio?

A For many reasons. I disagree with the use of the higher level term because it is such a broad group of terms from suicide ideation and all the way to attempts.

Even though you say serious suspect reports, I have to make -- there's no protocol. So I'm making the assumption that you're limiting it to those which Neurontin or Gabapentin was labeled as suspect, primary concomitant suspect drug. I'm sorry, primary or secondary suspect drug because it's not just primary suspect. There's deviation.

Q Understood.

A That's an assumption, though, but there's no protocol. So I'm not quite sure what you did.

Q Okay.

A Then you say serious. Just because it says serious, a suicide gesture, for example, or suicide ideation wouldn't meet the FDA definition of a serious adverse event.

Q Did you actually do a study of whether that's true or not?
A Excuse me?
Q Do you know if there are reports in the database where suicidal ideation is the only term which are marked as serious?
A I did not find one like that. But I did look at terms where there were suicide ideations and that they were serious and the drug Neurontin was suspect and I found there was quite a grab bag and it was pretty clear from review that the report wasn't a report of suicide ideation. It was reports of other events that wouldn't require hospitalization or meet the FDA regulatory definition of serious.
So this is really a grab bag of events that aren't necessarily related to the suspect or the serious classification. That's why I have some serious problems with using HLT.
Q When you said I did not find one like that, and that being a suicidal ideation report where that was the only term and that report had been sent in as serious, did you actually look to see if that happened?
A I did not look for that specific circumstance, no.
Q So there could be reports in the database

where suicide ideation is the only adverse event term that are marked as serious, correct?
MR. BARNES: Objection.
A I cannot see how that would meet the definition of serious by the Code of Federal Regulations.
Q But in analyzing and doing data mining, you're not looking at the individual reports, you are taking the data as it is as provided by the regulatory agencies, correct?
A With some cleaning. But that's why it's very good to base it on terms that make sense, not on just groupings of terms because they happen to be in the same HLT.
Q Did the FDA include suicide ideation in its meta-analysis?
A Did they include in the meta-analysis? Yes. They also said that they wouldn't use the spontaneous report data because for this drug and in this population it was not going to give them any information.
Q Were they talking about in the context of a causal -- making a causal assessment or were they talking about for any purpose whatsoever?
A They were talking about even for the case

of a signal. For generating hypothesis.
Q Where did it say that?
A Well, in Mosholder. Andy Mosholder's paper with Palmer they talk about that. I quote -- I reference that. Also in the adverse event report, Dr. Katz's letter to the advisory committee talks about the problems with spontaneous reports.
Q But he doesn't say you can't use it for signaling, did he?
A He said in this case that it was not of value.
Q The other terms that you complain about that are in the HLT, did you happen to look at how many times those other terms actually occur?
A Did I look? I might have looked briefly at the numbers on the HLT. But I didn't do any analysis on them, yes.
Q I'm not talking about HLT itself, but there are -- the HLT I believe is completed suicide, correct?
A That is in there.
Q Suicide attempt, correct?
A Yes.
Q Suicidal ideation, correct?
A Yes.
Q Depression suicidal, correct?

A I don't believe that's in there, no. I think that's in a different HLT.
Q I think you're right. Suicidal behavior, I'm sorry?
A Now I need to see it. But I believe it might be. It's five or six terms.
Q I believe it's top of page 24.
A Completed suicide, intentional self-injury, self-injurious behavior, self-injurious ideation, suicidal behavior, suicidal ideation and suicide attempt.
Q First of all, you say it's a mistake to include these intentional self injuries, correct?
A For the purposes of data mining I believe it should be done at the preferred term level and only look at events for the definition for serious. That's what I believe makes sense professionally.
Q So if a clinician thought that suicide ideation as the whole term in the report was a serious event, they were wrong then, correct?
A Are they using the FDA definition of serious? I mean, there's regulatory definition of what serious is.
Q If there are reports in the adverse event database submitted by manufacturers where the only term

is suicidal ideation marked serious, with one of the serious criteria, then are you saying those people are wrong?

A Again, if it met the FDA definition of serious, based on the legal definition of serious, that's amazing. I mean, I'm just surprised.

It would be, you know, require death, hospitalization, initial prolonged, congenital anomaly, life threatening. So I mean, these are the issues. Maybe there is a case, but I'm not going to hypothesize that.

Q Do you know if there are a lot of cases?

A A lot of cases in FDA --

Q In the FDA database where suicidal ideation is the only term marked as serious?

A I'm not aware of the number of cases or if there are any. That's hypothetical.

Q And you didn't look at Gabapentin to see if there were any cases of suicide ideation as the only event marked serious, correct?

A I looked at suicide ideation with Gabapentin. I didn't look for ones that just had that one term in them. I did find quite a few that had many terms, like 20 to 40 terms of which it was one of many terms.

Q Okay. But you cannot tell, just by looking at the terms selected, as to which one of the events caused the event -- which one of the terms caused the overall event to be considered serious, correct?

MR. BARNES: Objection. If you know, you can answer.

A In my report I go through a couple of cases where I found that there were some events which really by definition would be serious because they're life threatening like QT prolongation. Do I know the intent of the reporter? No. But it makes a lot of sense that that would be the reason of someone having a heart attack, a QT prolongation would meet the serious all the time.

But suicide ideation would not by itself meet the definition of a serious event.

Q If somebody put a gun up to their head and said I think I want to blow my brains out, is that a suicide attempt?

MR. BARNES: Objection. If you know.

A I'm not a clinical doctor. I believe it probably could be. Depending on the circumstances.

Q It could also be just suicide ideation, correct?

A I think it goes beyond ideation, even for a

lay person.

Q Well, is it an attempt?

A Again, I don't know. There's a fine degradation between these and I don't want to sit there and make a clinical judgment.

Q So somebody, a clinician, could consider that suicide ideation, correct?

A I don't want to make a clinical judgment.

Q I'm not asking you. I'm saying a clinician, who is there?

A That's a clinical judgment.

Q And they could call it a suicidal ideation, correct?

MR. BARNES: Objection. You may answer.

A That is a clinical judgment.

Q Okay. But you're making a judgment here that suicidal ideation is never serious and there you're willing to make that statement that it's never serious, but you're not willing to make a statement that it could be serious. I don't understand why it isn't a two way street?

MR. BARNES: Objection. Two different questions. You may answer again.

A In one case I'm talking about a report has a term. The term is not how seriousness or

non-seriousness is defined. It is defined by CFR that it is defined by the outcome; what happened to the patient. Not by what the event was. So there are some events that are, by their nature, serious. Particularly those events like suicide that result in death.

Q Isn't there also a category for where they reported things, while it doesn't meet one of those explicit definitions, they think it could lead to one of those outcomes?

MR. BARNES: Objection. Calls for speculation.

A What are you --

Q Do you know if there's a box on the MedWatch form for other?

A There is a box for other.

Q And that that box is to be used when in the opinion of the reporter the event, while not meeting one of the other conditions, death, et cetera, could lead to one of those conditions, correct?

A Box other does not have that clear a definition of how it's used. I find that it's used pretty broadly for just about anything.

Q Have you read the instructions to the MedWatch form?

A Yes.
Q MedWatch form specifically says that when the reviewer thinks that it could lead to one of those things, they can mark the other box, correct?
A Yes, other serious events.
Q So to make the statement that suicidal ideation is nonserious is not necessarily a true statement, is it?
MR. BARNES: Objection. Asked and answered. You can answer it again.
A By itself the term suicidal ideation does not mean that the patient had an event that met the FDA definition of serious. Conversely, if someone commits suicide, that does, by itself, just that term, automatically meet the definition of serious. That's what I'm telling you.
Q Okay. That's fine.
Would you look at how many reports of intentional self-injury were in the database?
A Did I look at --
Q For all drugs?
A I did not analyze those because I don't believe that those are going to tell me anything when I do a data mining exercise.
Q So it's your suggestion that intentional

of terms, like this HLT, then there's just -- you've got to include all the terms.
So there's other -- there's other preferred terms under other system organ classes, under other HLTs that are for example in the data capture rate that are suicide related. But they are not all -- depends, they're not all by definition serious. And again you need to make sure that a priori they're established, which a protocol is. It has to make sense. This doesn't make sense to me.
Q But if a clinician thought so, they could have good reason, correct?
MR. BARNES: Objection.
A In data mining and spontaneous report, I would have to say that might not -- I wouldn't necessarily agree. No.
Q Okay. You may object -- aside from disagreeing with whether it's HLT or not, whether you should use the HLT or not, does the data in between the black bars of Exhibit 25 suggest that there is a ratio greater than two, a chi-squared greater than 4 and you don't know the number of reports but assume for the sake of argument that anything that is 1 percent of the entire background of all events has to be greater than 4 reports?

self-injury has nothing whatsoever to do with suicidality?
MR. BARNES: Objection. You may answer.
A I'm not making a clinical definition. I'm not making clinical judgment. I'm data mining on two event terms that are used in the epidemiologic literature that are by definition serious.
Q Who picked those terms to use?
A I based it on the work done by Bentson McFarland who did an epidemiological study suicide and suicide attempt.
Q Did anybody tell you not to use suicidal ideation?
A No one told me what to do. I set my own protocol.
Q So if somebody with clinical experience felt that suicidal ideation should be looked at, as someone who is not a clinician and not a suicide expert, would you have the experience to dispute that?
MR. BARNES: For data mining purposes?
Q For data mining purposes.
A For data mining purposes I would talk to them and say that I want to make sure that the events that I look at are considered by themselves serious and if you're going to start putting together constellation

A Why does it have to be greater than four reports?
Q How many reports are there -- how many reports are there in the AERS database?
MR. BARNES: These are cumulative, correct?
MR. ALTMAN: Yeah.
Q At the point in time we're talking about, how many reports are there in the AERS database?
A Currently over 3 million.
Q What's 1 percent of 3 million? In '99, just between '97 and '99 would you say there's at least a million reports?
MR. BARNES: If you know.
A Probably about that because it's really grown over time.
Q What's 1 percent of a million, about 10,000?
A Okay.
Q That's a lot more than four, right?
A That's for the -- for all the drugs, right.
Q For all the drugs. So you don't have any real worry that 1 percent of the background is more than four reports here, right?
A I mean, it would be an assumption. But a reasonable assumption potentially.

Q I think we talked about the number of adverse event reports that the company got in '98 and '99. We looked at that earlier. It was in your report. Do you have any doubt that 2 percent of the reports is more than four reports?
A 2 percent of the reports?
Q For Gabapentin in 1999 represents more than four reports?
A Of serious suspect reports? I'd have to go look at the data. The numbers were pretty low at the beginning of marketing.
Q That's not the beginning of marketing, we're already five years into it?
MR. BARNES: She said she would have to go look.
A I'd have to go look.
Q Why don't you pull up in your original report, we talked about this earlier. We talked about how many -- I believe it is on page 16. I think we show in here in '98 you showed something about 700 reports?
A 1998.
Q I think we talked about was 700 reports; is that correct?
A Okay. About, yeah, between 5 and 600

probably.
Q And in '99 there's about 2,000 reports, right?
A Yes.
Q About 2,700 reports, right?
A In which year?
Q Between '98 and '99?
A In 1999 is about 2,000.
Q Do you have any doubt that 2 percent of those reports are more than four, any real concern that it could be less than four?
A But this is an apple and this is an orange, so. This is all reports that listed Gabapentin as either suspect or concomitant by year. That's not the same as what you have here. There's limited --
MR. BARNES: In Exhibit 25.
Q I agree.
A You have a limited subset and I don't want to speculate what the basic numbers are for your subset.
Q That's fine. Not a problem.
Top of page 21.
A Original report or supplement.
Q I'm sorry. Supplemental report. Top page. Only with careful clinical interpretation, considered

within the context of why the drug is being used, the extent of drug use, and background rates of the event, can a statistical alert be turned into what is considered a signal potential risk. Did I read that correctly?
A Yes.
Q Then you say at the bottom: I see no evidence that Dr. Blume or Mr. Altman enlisted proper medical experts to interpret their purported signal.
What's the basis of that sentence?
A There's nothing in the report that says that any clinical expert was enlisted to work with Dr. Blume to evaluate whether this chi-squared 6.70 P less than .01 with the Yates correction, whether or not that is clinically meaningful.
Q Did you review Dr. Blume's qualifications?
A Yes, I did.
Q Is it your opinion that Dr. Blume is not qualified to exercise clinical judgment?
A It is my opinion that she's not a clinician. I didn't see any medical degree, any nursing degree, any pharmacy degree. No clinical health professional degree in her CV.
Q And is it your opinion that only somebody with those degrees could possibly exercise clinical

judgment with respect to how to interpret safety data?
A I think someone for a clinical judgment, which is what we're doing, taking an alert for what you find as significant chi-squared value and you're saying that is something, which I disagree with. But taking that and making a clinical judgment I think requires a person with clinical expertise and expertise in AERS, yes, absolutely.
Q Do you know whether Dr. Blume felt there were signals long before 1997 with AERS?
A I only saw what she wrote in her report. I wasn't familiar with what she thought prior to 1997.
Q Did you read her report?
A Yes, I did.
Q Were you aware that a substantial portion of her report discusses what was seen in the clinical trials, did you review that information?
A I read everything in her report.
Q If Dr. Blume believed that there was information within the clinical trials themselves suggestive of a problem that should be investigated and monitored, do you have any basis to dispute that?
A I have no basis to agree with her. She has, as far as I can read, she has no clinical qualifications and so therefore I don't believe she is

qualified to make such judgments. She's not a clinical expert.

Q You say at the bottom of page 21 in the paragraph below that. Oh, actually, when we get above that. I'm not going to beat a dead horse over this.

But when you put -- I just want to be clear that I understand in your original chart there was some criticism in the original report that you were showing in the PRR as suicide and you showed it as zero. We had discussed that briefly and now I think you said that zero is the software's default value, is that correct? When it cannot calculate a PRR?

A Right. So in other words until it moves above zero there's not a calculated PRR. But I wanted to make sure that it was clear that I looked at that time period because if you noticed I graphed both completed suicide and suicide attempt together. And there were cases of suicide attempt in that early time period. I didn't want to mislead people looking at the graph and that's why it's at zero.

Q But somebody looking at that graph would be misled to believe that there were no suicides in Neurontin at the same time there were suicides in the background, correct, which is the only way you could get a PRR of zero?

reports of suicide in the background but no reports for the drug of interest. What percentage of the reports for the drug would be if there was zero reports for suicide?

A Excuse me?

Q If there were zero reports of suicide for the drug, what percentage of reports would that be?

A If there was zero?

Q Right.

A Zero.

Q If there were some reports in the background, regardless of what the background is, that would not be zero, correct?

A Right. Something divided into zero.

MR. BARNES: Zero into X, is what you're saying, right? It has to be some value greater than zero.

Q Which is zero, correct?

A Okay.

Q But that's not the same thing as undefined, is it?

MR. BARNES: Under what program and what assumptions?

Q Not any program. If you show somebody a PRR of zero, the only way you can get to zero when you

A You could get -- based on the way that it's a default, you could get a zero if there's nothing in the foreground or in the background. That's the default. If you can't calculate it, it's a zero.

Q Forget about Q Scan. Somebody looking at that chart who says this is the PRR as graphed, you graphed the PRR as zero, the PRR was not actually zero, correct?

A The PRR was zero as far as I'm concerned. There was no calculatable PRR. It is not misleading. I think it would have been misleading to not put something there because it would look like I hadn't started my calculations at time zero.

Q If there were no reports for the drug, no suicide reports for the drug, but some suicide reports for the background, wouldn't that also give you a PRR of zero?

MR. BARNES: Objection. Do you understand the question?

A Yeah, I'm thinking.

MR. BARNES: Ask it again.

A I'm thinking, I'm thinking calculation here. Nothing for the drug. It's not calculatable if you don't have something for the drug.

Q Why is it not calculatable? You have some

truly calculate a PRR is if there are no events for the drug versus some events for the background, correct? It's the only way zero can come up in the calculations?

A As I stated here, I state in the report, the zero on my chart was that there was nothing there. It's the default for not calculated or not calculatable. That's all it is. I want to make it very clear for the record that that is what it is. If you misinterpreted it, I'm very sorry, but that was not the intent.

Q So you're saying that somebody looking at that chart would understand that it was zero because it was a default value with the absence of your supplemental report?

A I believe they would or if they didn't, they would ask.

Q You say in the last full paragraph, the suicides and suicides attempts --

MR. BARNES: What page?

MR. ALTMAN: I'm sorry, we're on 21.

Q It says: The suicides and suicide attempts from COSTART were mapped to the major PT suicide attempt. Did I read that correctly?

A Yes.

Q That means that some of the suicides, and

just to go back, there was no term for suicide back in the COSTART era prior to the AERS, correct?

MR. BARNES: I don't think that's right.

Q There was no term for completed -- there was no term for completed suicide in the COSTART dictionary, correct?

MR. BARNES: Don't guess. If you don't recall.

A I'd have to go back and look at the HL in my code. I believe it's in my -- it's in one of my exhibits that I looked at, the COSTART coding dictionary.

Q Okay. Well, we discussed this last time. I'll represent to you there is no term for completed suicide in the COSTART dictionary.

MR. BARNES: Objection.

Q You show evidence of that because you say the suicides and suicide attempts from COSTART were mapped to the major term suicide attempt. Why would you map. If it was a completed suicide, why would you map that to suicide attempt if you could tell that it was a completed suicide?

A There are many situations in the mapping of COSTART to MedDra where a term in COSTART is coded to a more generic term in MedDra.

Q Okay. On 24 when we were talking before about the HLT, did you happen to look at what effect of the numbers including intentional self-injury, self-injurious behavior, self-injurious ideation in the HLT had on the percentages and calculations using the HLT?

A I didn't look at percentages.

Q Did you have any impact -- do you have any understanding of how that impacted the PRR as you calculated it?

A Can you repeat that?

MR. BARNES: She used preferred terms.

MR. ALTMAN: She also said that she calculated HLTs. But I'm asking how it would have impacted.

Q Do you know what percentage, if you take suicidal and self-injurious behaviors and HLT, do you have any idea what percentage of those reports are distinctly intentional self-injury, self-injurious behavior or self-injurious ideation?

MR. BARNES: Objection, if you know.

A No, I don't.

Q If I told you it was between 2 and 3 percent of the reports, would you have any basis to dispute that?

MR. BARNES: Objection. Calls for speculation. You either have personal knowledge or you don't.

A Percentage of what reports?

Q If you take all of the reports of suicidal and self-injurious behavior in the entire FDA database and you look at how many of those reports only have self-injurious behavior, self-injurious ideation or intentional self-injury, that represents about 3 percent of all of the reports of suicidal and self-injurious behavior. Do you have any basis to dispute that?

MR. BARNES: One way or the other she says she hasn't looked at it.

A I have no basis at all. I haven't looked at that.

Q Do you think that 3 percent of the reports that may or may not be related could substantially alter --

A I don't understand what you're talking about.

MR. BARNES: Objection.

A It makes no sense.

Q We'll move on.

See at the top of page 25. You say, even

if there were a signal in 1994, and I just want to verify you did not do anything to review whether there was or was not a signal in 1994, correct?

A That's incorrect. I did the data mining to go back from day one.

Q So once again --

A So there was no statistical alert. If there's no statistical alert it doesn't take you to the next step to see if there's a signal.

Q But as we said that's assuming that you have to use data mining to determine signals. So you're not saying the general proposition that there might not have been a signal based on case reports or clinical judgment, correct?

A If there was nothing on the Parson's report, then it's a pretty good assumption there was nothing prior to the Parson's report because they looked at all of the data from the beginning of marketing, so.

Q They only looked at data on suicide, suicide attempt and suicidal ideation, correct?

MR. BARNES: Do you need to see the report?

A I would have to go back to the original report.

Q I'm going to mark as an exhibit -- I

believe we're at 26.

(Whereupon, a document was marked as Deposition Exhibit Number 26.)

Q This is a really, really new document that frankly was just made available probably on Tuesday of last week which represents the FDA's -- the letter that the FDA is sending to all the manufacturers of antiepileptic drugs in response to the analysis in the advisory committee. Have you had to see this document prior to today?

A Not this version of it.

MR. BARNES: Why don't you take some time and read through it.

Q I'm going to ask you very little about it. We're not going to get into the gory details of it.

Really what I'm going to ask you about is on page 8 in the proposed medication guide. It's not proposed, I think this is the medication guide.

MR. BARNES: The medication guide prepared by FDA.

MR. ALTMAN: Prepared by FDA which I believe is what will be required of all manufacturers.

(Witness reading.)

MR. BARNES: We'll object to this as being a unspecified document sent out to -- I guess publicly,

Q Yes.

A Okay. There's page three, here's page numbers.

Q It's the medication guide.

A Okay. Page eight.

Q Call a healthcare -- point 2 it says: Call a healthcare provider right away if you have any of these symptoms. Especially if they are new, worse or worrying you. Did I read that correctly?

A Yep.

Q Would you please read in that list?

A Thoughts about suicide or dying; attempts to commit suicide; new or worse anxiety; feeling agitated or restless; panic attacks; trouble sleeping; insomnia; new or worse irritability; acting aggressively, being angry or violent; acting on dangerous impulses; an extreme increase in activity or talking, mania; other unusual changes in behavior or mood.

Q Does this document list things other than simply suicidal ideation or attempts?

A Yes. It's quite a long list.

Q So according to the FDA new or worse depression should also be looked at, correct?

MR. BARNES: Objection. That's not what it

which is not specifically been proposed on Neurontin or gabapentin. Although I'm not denying it wasn't sent to them. But I'm not accepting your assertion that this is what the FDA will require at this point.

MR. ALTMAN: That's fine.

THE WITNESS: I haven't seen this document before.

MR. BARNES: We're not stipulating as to actually any aspect of this medication.

MR. ALTMAN: I will represent this is what is publicly available on the FDA web site which I personally downloaded and provided to you.

MR. BARNES: What I'm saying -- I'm just saying we're not accepting the information in here is specifically applicable to Neurontin.

It's a medication guide that's on the web, but this may not be the medication guide for Neurontin because the numbers in this don't even relate to anything that has to do with Neurontin as far as I can tell. I haven't seen this before.

MR. ALTMAN: That's fine. I understand your concern.

BY MR. ALTMAN:

Q On page eight --

A Page eight?

says.

Q Okay. Is it correct, that's what it says?

MR. BARNES: No, it says call a healthcare provider.

A Call a healthcare provider.

Q If you have symptoms of new or worse depression, correct?

A If you have any of these symptoms, especially if they're new, worse or worry you.

Q And one of them is new or worse depression, right?

A That's on the list.

Q So according to the FDA and this is an alert talking about suicidality, correct, the entire document?

MR. BARNES: It's a medication guide. It's not an alert.

Q It's a medication guide. But the whole topic of this medication guide and the documents here are talking about suicidality associated with antiepileptic drugs, correct?

MR. BARNES: Objection. Misstates and mischaracterizes the document. And you're asking her to assume what FDA's intent was.

MR. ALTMAN: I'm not asking her to assume

anything.
MR. BARNES: Yes. Reask your question and listen to it again.
Q Go to the bottom of the first page.
MR. BARNES: The medication guide?
Q No, the first page of the entire document.
A Okay.
Q It says: After considering all relevant information, including the new safety information, we believe that the new safety information --
A Where are you?
Q At the bottom -- we believe that the new safety information should be included in the labeling of, insert name, and we have determined that a REMS is necessary for the drug to ensure that the benefits of, insert name, outweigh the risks.
Did I read that correctly?
A You read it correctly, but it doesn't make sense in light of the safety information, the study that they did. This is not supported by the study.
Q So you disagree with the FDA, correct?
A I disagree with this one on the FDA. I think they've misinterpreted their study and it has some flaws. Seriously misinterpreted it.
Q That's fine. But this is what the FDA has

included this large list of symptoms.
Q Is that the first time the FDA ever used a list like this?
A I do not know offhand.
Q Do you know if in the original alert there was a listing of symptoms that were of concern?
A I'd have to go back and refresh my memory.
Q Okay. Before we move off this, would you consider an intentional self-injury to be a dangerous impulse?
A I don't want to make a clinical judgment.
Q Okay. But just to be sure, you did make a clinical judgment in deciding not to include intentional self-injury in the terms for data mining, correct?
A That wasn't a clinical judgment. That was a methodologic decision based on adverse event reporting.
Q So I'm not sure I understand why you didn't include intentional self-injury then?
MR. BARNES: Objection. Asked and answered. Tell him again.
A Again, I limited to those events that were A, by themselves serious by definition and that those are the two. I didn't want to include a grab bag

decided, correct?
A I don't know. I haven't seen this document that you've given us today. I don't know what stage it's at.
Q If this document is being sent out to all manufacturers of antiepileptics, this is the FDA's decision, correct?
A I don't know if this is the document that's finally getting sent out. I don't know what stage it's in.
Q If the FDA has it on their web site and says this is what we're sending out to manufacturers, do you have any basis to dispute that?
A I have no basis either way. I haven't seen it before today.
Q Okay. Assuming that this is the document that the FDA is sending out, which I will represent to you is what they have told the world in making it a public record, does it appear that on the medication guide page two there are other symptoms that the FDA has decided is relevant to the question of whether somebody will commit suicide?
MR. BARNES: Objection. Assumes facts not in evidence as to what FDA decides.
A I don't know in what context they've

events. I wanted to be very specific.
Q Do you know?
MR. BARNES: Let her finish her answer.
Q I'm sorry. I thought you were done.
A That's very important with this because it's adverse event reporting. There's a lot of inherent biases.
Q Do you know if when you did your calculations, your charts here, as we have discussed before, you calculated one ratio and another ratio and the two were divided together, that's how you got your PRR; is that right?
A That's essentially what it is.
Q Your denominator you were very important you wanted to use serious reports, correct?
MR. BARNES: Objection.
A I didn't limit it to serious reports.
Q Well, suicide and suicide attempt?
A I limited it to those serious events. So those two events.
MR. BARNES: For the denominator or numerator?
MR. ALTMAN: For the numerator.
MR. BARNES: Your question is denominator.
Q I'm sorry. Your numerator was limited to

serious events, correct?
A My numerator was limited to suicide and suicide attempt.
Q By the way, do you know if there were any suicide attempts that were marked as nonserious?
A Didn't look at that.
Q But presumably -- did you presume that suicide attempt would be serious?
A I presumed that it would be clearly reported more so than some of these more nefarious kind of terms. So yes, that is why I used it.
And, two, it's also used in the literature. It was part of Bentson McFarland's paper, Suicide and Suicide Attempt. Those are two reports that were reasonable to get from large databases. So I believe they're reasonable to look at.
Q Are suicide attempts serious?
A I believe they can be.
Q Are they always?
A Clinically, I don't know about every single scenario. So I'm not going to make that judgment. But I would assume that it probably is very serious when someone makes an attempt to kill themselves.
Q In your denominator did you include nonserious reports?

A I included all reports in my denominator.
Q Top of page 25. I think we were talking about, let's see, even if there was a signal in 1994, we looked at in the letter from the FDA that there are other terms listed there in the medication guide concerning suicidality and antiepileptic drugs. We looked at that before.
Do you know if there were issues with other adverse event terms besides suicide and suicidal ideation from a clinical perspective in that timeframe?
A I'm not quite there I understand what you're saying.
Q You refer to the Parson's report which only looked at suicide, suicide reports and suicidal ideation. Parson's report didn't look at depression, correct?
A I don't believe it did. I have to go and refresh my memory.
Q It didn't look at anxiety, correct. Is that correct?
A Do you have a copy of it?
Q I don't.
A I'd like to see it.
Q I don't.
MR. BARNES: If you know, please answer.

A I can't remember. I would have to actually look at the report. It's been a while. We did this a year ago.
Q Okay. That's fine.
We talk about the gabapentin data capture rate and you said it wasn't feasible to use the gabapentin data capture rate back in 1994; is that correct?
A I don't believe it was feasible, yes.
Q Could you have done -- used something like the gabapentin data capture rate using terms that were in use in 1994?
A It's my understanding that this concept didn't exist in 1994. A lot of this came out of the work out of Columbia University which was published much later. It didn't come out until they were doing the studies of suicidality and SSRI. So this concept of suicidality didn't exist way back when in the way it does today.
Q The company was coding reports as completed suicide back in 1994, correct?
MR. BARNES: Objection.
Q Internally?
MR. BARNES: Objection. If you know.
A I did see reports that were coded with

completed suicide in them.
Q So they were not limited by, internally, the company was not limited by COSTART, correct?
A I don't want to make an assumption. I don't know what the limits were on the company in 1994.
Q Do you know if the company was required to use any particular dictionary in conducting it's pharmacovigilance activities?
MR. BARNES: What time period?
Q In 1994.
A If they were required? I'm not aware of what the requirements were in 1994.
Q Have you ever reviewed the guidance for industry on post-marketing safety for guidance reporting?
A Yes, I have.
Q Could the company have used a different set of terms if they wanted to monitor psychiatric, concerns of psychiatric adverse event associated with use of Neurontin?
MR. BARNES: Different from what, Keith?
MR. ALTMAN: Can I finish?
Q And done conceptually the same things they were talking about doing with the data capture rate, which was to look at a collection of terms together?

MR. BARNES: Objection. Assumes facts not in evidence as to what the gabapentin capture rate was supposed to -- its purpose. You can answer.

A I'm saying this specific data capture rate involves concepts that weren't, in terms that weren't in use in 1994. What else they could have done, I don't want to surmise.

Q You also mentioned that she didn't include intentional overdose when she did her analysis. I believe that's on page 24. Is that correct? You say two additional terms which she missed were intentional overdose and deliberate poisoning. Do you see that? It's about the middle of the paragraph?

A Uh-huh. I do see that.

Q Would it have made sense to look for disproportionalities with Neurontin using the term intentional overdose at the PT level?

MR. BARNES: For what purpose?

A In what context?

Q Are you aware that many people who used Neurontin used it at a higher dosage than was approved by the FDA?

A No, I'm not aware.

Q I want you to assume that the evidence will show that that's, in fact, true. Would some of those

potentially have an adverse event associated potentially have included --

THE COURT REPORTER: You have to repeat that question again.

MR. ALTMAN: Sorry.

Q I want you to assume that the evidence will show that is in fact true that many people used Neurontin at dosages higher than approved by the FDA. If an adverse event occurred associated with that use, might the reviewer -- might the company have coded it also as intentional overdose because they took a dosage greater than that approved by the FDA?

MR. BARNES: Objection. Vague as to many. Assumes facts not in evidence. Lack of foundation. If you can answer that, go ahead.

A I don't know how I could answer that question.

Q Okay. So you don't know whether there was good reason to not use the term intentional overdose in performing data mining activities?

A You're taking my words out of context. Here what I'm talking about is Dr. Blume justifies her use of the HLT by saying it's exactly the same thing as in the data capture rate which is just everything I use, plus a few other terms. But it's more than that.

She only uses 60 percent of the terms.

So I wanted to be very clear to say that the premise that she's basing her statement on is in fact incorrect. It is not the same thing.

Q Okay.

A Six out of 10 terms is not the same thing as 100 percent of the terms.

Q Let's go to page 27. Bottom paragraph, second sentence. Mr. Altman states that PRR analysis can generate a "signal of a safety problem that when combined with other information supports the conclusion that Neurontin has the biological capacity to cause patients who take it to commit or attempt suicide." Altman declaration 2008 paragraph 27. Did I read that correctly?

A That's what I wrote here.

Q In putting that in double quotes, are you telling the reader that Mr. Altman, who is me, makes that statement as if it is his statement?

A I'm putting quotes that is what I got out of your declaration on paragraph 27.

Q And you would lead a reader to believe that that is what I, Mr. Altman, states as if it is my statement, correct?

MR. BARNES: Objection. Misstates her

testimony.

Q Let's go off the record. Change the tape.

THE VIDEOGRAPHER: We're going off the record. The time is 5:14 p.m. This is the end of tape number 6.

(Off the record.)

THE VIDEOGRAPHER: We are on the record. The time is 5:26 p.m. This is the beginning of tape number 7.

BY MR. ALTMAN:

Q Okay. I'm going to mark what's Exhibit 27.

(Whereupon, a document was marked as Deposition Exhibit Number 27.)

Q Have you seen Exhibit 27 before?

A It looks familiar.

Q I believe that's what you're talking about at the top of page 28; is that correct?

MR. BARNES: The supplemental report.

Q The supplemental report, sorry.

A Is this Exhibit C? Can you verify that? Altman Declaration 2008.

MR. BARNES: I'll take Mr. Altman's --

MR. ALTMAN: Let's be sure.

MR. BARNES: -- reference to that. I believe it's Exhibit C. He can tell you. I'll take

his representation as to --
MR. ALTMAN: Yes. It's Exhibit C.
MR. BARNES: Page 28 at this point.
MR. ALTMAN: That's correct.
MR. BARNES: Okay.
BY MR. ALTMAN:
Q Now, you comment -- first of all, have you ever seen any analysis ever performed by the company of any kind at any point in time that reviewed adverse events broken out specifically by different occasions?
A I don't recall.
Q Okay. You suggest here that this is an example -- this graph purportedly shows an increase in the percentage of serious adverse event reports for suicidal and self-injurious behavior associated with psychiatric indications; is that correct?
A Say that again.
Q That this graph graphs the percentage of serious adverse event reports of suicidal and self-injurious behavior for various different indications, correct?
A Purported that's what it says.
Q You comment upon the fact that there is an increase in the psychiatric curve and you say his work clearly illustrates -- his work clearly illustrates the

importance of considering confounding by indication. Suicidal behaviors expected to be higher among patients who are being treated for psychiatric conditions than epilepsy and other indications. Did I read that correctly?
A Yes.
Q Is one possible explanation for that increase that people who take Neurontin for psychiatric conditions use the drug and it has no efficacy and that the person just did what someone -- an untreated person might do if they don't receive treatment?
MR. BARNES: Objection.
A I'm not making those assumptions.
Q Is that a possible explanation of why you see that increase?
A I have a lot of questions about this graph before I would actually be able to interpret it.
Q You comment upon the increase in the curve for psychiatric conditions, right? You say that shows demonstrates confounding, correct?
A I said, your work clearly illustrates the importance of considering confounding by indication.
Q And then you say -- you say suicidal behavior is expected to be higher amongst patients, correct, who are -- psychiatric conditions, right?

A Yes.
Q Now --
A That's based on the literature, not based on your graph.
Q Understood. The question is, is that, if there's an increase in the percentage of suicidal and self-injurious reports for psychiatric conditions, there are many explanations as to why you might see that, correct?
MR. BARNES: You mean hypotheses or explanations?
A Could you repeat that?
Q Possible explanations as to why you see this graph, correct?
A There are many possible explanations. You have to go back and first say is this true and if it's true.
Q I'd like you to assume for the purpose of our discussion that this chart is accurate?
A Of what data?
Q Of -- this is of companies -- companies' internal AIRS G data, which you didn't look at, but that these percentages are accurate based upon the data?
A I'd have to make an assumption. I don't

know.
Q I'd like you to assume that, but you have no basis for saying that that's not true because you didn't look at the data, correct?
MR. BARNES: You're asking her -- say what you want her to assume again.
Q I just want you to assume that the numbers here are numerically correct?
MR. BARNES: Okay.
A I'll make an assumption.
Q And that's fine. This chart does show that the percentage of reports of suicidality, suicidal and self-injurious behavior for people who took Neurontin for psychiatric conditions is higher than the other indications, correct?
MR. BARNES: It's a greater percentage.
Q It's a greater percentage, correct?
A Percentages of serious report --
(Witness reading.)
A Now is this only amongst serious reports?
Q Yes.
A Are these the denominator and the numerator or just the numerator?
Q This is only serious reports.
A Among all the serious reports?

Q -- of serious reports, correct. So, for example, if you take June 30th, 2006, the chart shows that about 9 percent of the serious reports for people who took Neurontin for -- where psychiatric conditions were indicated with suicidal and self-injurious behavior --

A What time point?

Q June 30th of 2000, I'm sorry 2000, 6/30. June 30 of 2000. 9 percent.

A Okay. And?

Q Does this chart show that a higher percentage of people taking the Neurontin for psychiatric conditions had an event of suicidal and self-injurious behavior?

A No, it does not.

Q A higher percentage of reports were of suicidal and self-injurious behavior?

A Could you repeat the question, please?

Q Does this chart show that a higher percentage of reports of people taking Neurontin for psychiatric conditions had an event of suicidal and self-injurious behavior?

A One more time.

Q Does this chart show that a higher percentage of reports of people taking Neurontin for

Q I'm telling you that at 2000, 6/30, June 30, 2000, 9 percent of the serious adverse event reports where the indication was a psychiatric condition contained a term for suicidal and self-injurious behavior. Okay?

A In which the indication was specified as psychiatric.

Q As psychiatric?

A That is what I believe this is telling me.

Q And for antiepileptic at the same time in point it appears to be about 1.6 percent; is that correct?

A Antiepileptic? It's hard to say, but yeah, somewhere about 1 percent maybe.

Q I'm sorry, you're right, a little above 1 percent, correct?

A 1 percent of the serious reports had HL -- one of these HLTs in there.

Q Right.

A Among those who specified an outcome, antiepilepsy.

Q Right.

A Okay.

Q Now if you look at this chart, what it shows is that the percentage for psychiatric conditions

psychiatric conditions had an event of suicidal and self-injurious behavior?

A Higher than what?

Q Than the other indications on this chart?

MR. BARNES: The issue here, maybe you can help us, just for the record, when you look up -- all the percentages here do not add up to 100 percent. So it's difficult for -- to answer that question. When you look at it, you only have, like, 25 percent of the -- you add up all these things and you've got much less than --

Q I'll go at it a different way. If you take a look at 2000 June 30, 6/30?

A Okay.

Q This chart shows that 9 percent of the serious reports where the indication was psychiatric conditions with suicidal and self-injurious behavior.

A Were these only among the psychiatric conditions?

Q 9 percent of the people who took it for psychiatric indications, where that was indicated in the database, is for a psychiatric condition. Okay?

A Not yet.

Q All right.

A Not yet.

is higher than any of the other conditions, correct?

A Well, because I don't know the N's and --

Q Just the percentage, I'm not asking about N's. The percentage is higher, correct?

A But it could be one out of 2 or 1 out of 10. So it may not be meaningful.

Q But the percentages are higher?

A The percentage are different. I don't know how meaningful they are because I don't have access.

Q But is the percentage higher for psychiatric conditions than the other conditions?

A The percentage is different, yes.

Q Are they higher?

A 9 percent is higher than 1 percent, yes.

Q And at the data point before is it also higher at June 30th of '99?

A Again, I'm not sure about the significance of it. Whether it's statistically significant, the underlying N's. We could be talking about three cases here. But the numbers -- the percentages are different.

Q And, in fact, at every point after 1999 on this chart the psychiatric conditions is higher than the other curves, correct?

A Was this zero over zero or? You have some

zeros here. Zero percentages.
Q No, that means there are no suicidal and self-injurious reports -- no serious for psychiatric conditions at that point in time?
A Thank you.
Q It's zero. It's not zero over zero. It means zero. It's not undefined. It's zero.
Anyway, but at every point after 1999 the percentage for psychiatric conditions is higher, correct, than any of the other indications?
A After 1999?
Q June 30th of '99, that data point. Everything is higher, correct?
A The percentages are higher for that subgroup.
Q Now, is one explanation for that observation that these are people with psychiatric conditions and people with psychiatric conditions tend to commit suicide more than people with these other conditions?
A I would say very strong possibility.
Q That's one possibility?
A That they have a lot of underlying conditions. They may be treated because of that very reason.

Q Is it a possible that that's what's going on, that Neurontin has no efficacy?
MR. BARNES: Objection.
A It's not a reasonable assumption based on this chart.
Q Is it possible that Neurontin actually is causing harm?
MR. BARNES: Objection.
A Based on all of the data that I've seen, there is no evidence at all that Neurontin is causing harm.
Q But you've never looked at the data by indication, correct?
A I looked at the FDA analysis which they looked at the indications for the trial and this is absolutely not what they saw.
Q They did not look at spontaneous data, correct?
A Right, because they don't believe that the spontaneous data has any validity for looking at this outcome because of the confounding indication which is probably what you're seeing here.
Q But that's speculation --
MR. BARNES: Objection.
Q -- that's probably what you've seen,

Q That's correct.
A High risk.
Q That's what we talk about with confounding indication, correct, confounding by indication; is that correct? That's what you were talking about?
A Yes.
Q Now, is another possible explanation that Neurontin had no efficacy for these people and so basically you were dealing with people who had psychiatric conditions who were not receiving any treatment and they committed suicide?
MR. BARNES: Objection. Assumes facts not in evidence and --
A It's way beyond what I can take from this chart. We don't have anything about efficacy. We don't have anything about whether they're on other treatments. And I would expect a lot of them are on other drugs, from what I've seen.
Q I just asked if one possibility is that Neurontin is not efficacious for these people?
A It's so far beyond what this shows, that's a real big leap.
Q Is it a possibility?
MR. BARNES: If you --
A For everybody? I can't imagine.

correct?
A Confounding by indication is the biggest problem we have in pharmacoepidemiology, and it's the first thing one considers when they're looking at spontaneous data or observational data in general. So it's a pretty good guess. This looks pretty clear.
Q Is it also possible that the drug is actually causing people to commit suicide based on this chart?
MR. BARNES: Objection.
A Based on this chart, you can't take that leap.
Q But you can take the leap that it's confounding by indication?
A That is the first explanation that I would consider when I look at this because if it's biological you would expect the rates to be up on all the groups.
Q What?
A You would expect the rates to be elevated on all the groups. Why would you expect --
Q So is it your opinion that drugs affect every population of people the same way. That they don't have different effects depending on a particular population?
A Can you clarify that.

Q Sure. Are some drugs contraindicated to people are who allergic to a substance within the drug?
A They can be.
Q So for that particular population, there is a risk that is different in using the drug than for people who are not allergic to the drug, correct?
A An allergic response, yeah.
Q The risk is different for that population, right?
A The risk of having an allergic response is different. It's not zero in the people that haven't had a previous allergy, but it is lower.
Q But there's a different risk, correct, there's a risk differential?
A Right. Everyone has the risk, but the likelihood may be different.
Q How do you know that people who are bi-polar don't have a different risk in using Neurontin than people who are epileptic?
MR. BARNES: Objection.
A I have no evidence to base that on.
Q But you don't know one way or the other, correct?
MR. BARNES: Objection.
A I know from the literature that there's

determine that Neurontin does not have a risk of suicidality to a bi-polar population?
A It's not adequate to show that it does. It doesn't show anything.
Q And can you conclude from that that there is not a differential risk for people who are bi-polar in using Neurontin and for people who are not bi-polar?
A But if there isn't a risk, how can there be a differential risk?
Q Differential risk generally. Not just of suicidality. In seven patient years of exposure, would you be able to determine that Neurontin is safely being used in a bi-polar population?
A I don't know that. It's based on FDA regulations and what is an adequate and well-controlled trial. I don't want to make suppositions of what was and wasn't adequate well-controlled trials.
Q But you're aware that Neurontin does not have a bi-polar indication, correct?
A I'm aware of that.
Q And that they never submitted an application for bi-polar, correct?
A I don't know whether or not they ever submitted an application. I'm aware it does not have a labeled indication.

differential baseline risks regardless of treatment. But there's no evidence that Neurontin changes the risk. There's some evidence actually that may decrease the risk of suicidality.
Q But in the clinical trials, there was only about 10 or 12 patient years of exposure, correct?
A 10 or 12?
Q 10 or 12 patient years of exposure for bi-polar, correct?
A I don't recall the numbers of patients with exposure.
Q If I told you 945209 that there was seven years of patient exposure, this was listed in the Parson's report, do you have any reason to dispute that?
A I just have to go back and verify it.
Q Would you consider seven patient years of exposure adequate exposure to determine whether Neurontin presents a risk of suicide to a bi-polar population?
A Just that of itself?
Q Well, if there's -- that's the only clinical trial in bi-polar in randomized clinical trial in a bi-polar population and you have seven patient years of exposure, is that adequate exposure to

Q And therefore the FDA has never said that Neurontin is safe and effective for use in the bi-polar population, correct?
A It is, from what I've learned and there was of a wonderful article just published this month, that there are quite a few drugs that are used in bi-polar that are not labeled and they suggested that bi-polar disease is -- and the drugs being used are one of the priorities for research.
MR. ALTMAN: Objection. Nonresponsive.
Q Therefore, the FDA has never said that Neurontin is safe and effective for use in the bi-polar population, correct?
A I don't know if the FDA has ever evaluated Neurontin for bi-polar population.
Q How much is 100 percent increase from 10?
A Oh, I'm tired.
MR. BARNES: Take your time. It's been a long day.
A Yes. A relative risk.
Q We're not talking relative risk.
MR. BARNES: Reask the question.
Q How much is a 100 percent increase from 10?
A It doesn't make sense.
MR. BARNES: Why don't you put it in

context.
Q 10 increased by 100 percent is how much?
A Add two zeros.
Q Not multiplied. 10 increased by 100 percent?
A 10 or 10 percent?
Q If 10 is increased by 100 percent, is that equal to 20?
A 10 doubled, yeah.
Q On paragraph three of your report on page 28 you say that a 174 percent increase from 212,978 to 370,898. Did I read that correctly?
A Uh-huh.
Q Is that 174 percent increase?
A Do I get a calculator?
MR. BARNES: Do you want to give her a calculator?
A It's late.
Q 174 percent increase would be more than doubled, correct?
A Can I get my calculator. I'm not doing this --
Q That's fine.
A It's not working.
Q 174 percent increase implies more than

you're aware that that point in time is actually November of 1997? Are you aware of that?
MR. BARNES: Where are you?
Q You say: Mr. Altman compares the number of completed suicide event reports from 1997 to 2002. Did I read that correctly?
A Yes.
Q I'll represent to you that was really from 1998?
A I believe you started in 1997 when AERS started; is that correct? November 1st of 1997.
Q November of '97, okay. Given that, that's about a -- just over a five-year period of time, correct?
A Yes.
Q And if there were eight reports, how many reports per year is that to the FDA, so 1.6 --
A One and a fraction each year.
Q 1.6, does that sound right?
A About that.
Q First half of 2003 there were 17 reports to the FDA, correct, or that's what it says?
A That's what you purport, yes.
Q And that's 34 per year, correct, 17 and a half a year is 34 per year?

doubling, correct, based on what we just discussed?
A I want to check my numbers. But I can't do it, I apologize.
Q I'll represent to you it's a 74 percent increase and --
MR. BARNES: Probably a typo.
Q -- not 174 percent increase. Does that seem reasonable?
A Yeah, I mean, like I said, I want to check my numbers.
Q If it's a 74 percent increase, then you're off by 100 percent?
A Okay. I apologize for the typo. Thank you for pointing that out. I'll have to doublecheck that number.
Q Do we know whether there are other mistakes like that within this report and within the computations?
A I try and be very careful. It's a big report and you tell me. You probably went over it with a fine tooth comb.
Q That's my job.
A Yep.
Q Second paragraph, page 28. You say: Suicide events reported from 1997 to 2002, correct,

MR. BARNES: Objection.
A I think I made it very are clear in my report that the numbers of events -- the reports were not constant in that year. That it was significant increase from the first half to the second half of the year.
Q But we're only talking about the first half of the year?
A Right, but you actually doubled it in your calculation and assumed that it was constant over the year, which was not a reasonable assumption.
Q Well, it was much more than 17 the second half of the year, wasn't it?
A I can't remember what the numbers are. I'd have to look in the report.
Q But if there was something that changed in the second half of 2003 that could have biased the reports, would you want to exclude that period of time so that you might be able to take that bias into account?
A That's if you can definitively say when the notoriety bias began and I would say that you can't because there's all sorts of issues, particularly with suicidality, with all the publicity with the SSRIs for the two years before that.

Q That's pure speculation whether that affected gabapentin, isn't it?
A No, a lot of the drug use for gabapentin includes concomitant use of SSRIs. People use antidepressants and other drugs. So it's not speculative that they would be used concomitantly.
Q But in terms of reporting to Pfizer, you're assuming that that's influence reports being reported to Pfizer, correct, and not to the SSRI manufacturer?
A I think it affects adverse event reporting in general.
Q Do you know what the source of the 17 reports were?
A I believe these were poison center reports from the literature.
Q Do you think those were affected by notary bias?
A I think they were accumulated over a long length of time.
Q Because Pfizer didn't look at reports --
MR. BARNES: Objection.
Q -- they looked at all of those reports at one point in time, right?
MR. BARNES: Objection. Assumes facts not in evidence.

Q Was Pfizer -- these reports were accumulated over a period of time, correct?
MR. BARNES: By whom? By the poison center?
Q By the poison control?
MR. BARNES: That's a different question.
Q These reports didn't all come from one annual report of the poison control centers, right?
MR. BARNES: If you know.
A I can't remember whether they came from just one report or several reports.
Q I'd like you to assume that they came from multiple reports, multiple annual reports that were looked at at a period of time. Do you have any evidence that those were influenced by your SSRI bias?
A These specific reports?
Q Yes.
A No, and I don't have any evidence that they weren't separately reported to the drug companies.
Q But we're talking about what Pfizer knew and not what went to other companies. This is only in terms of Pfizer's own data?
A This isn't Pfizer's data, this was in the medical literature.
Q But this is data that was reported by

Pfizer to the FDA?
A Right, because they're required to monitor the literature.
Q Understood. So Pfizer became aware in the first half of 2003 there were 17 suicide reports from the poison control centers; is that correct?
MR. BARNES: If you know.
A I believe that is correct. I have to look at the reports.
Q And you don't have any evidence that those reports were influenced by this SSRI bias you discussed, correct?
MR. BARNES: Objection. If you know.
A I don't know. Personally.
Q I want to read you some statements and see if you agree with them. Risk assessment during product development should be conducted in a thorough and rigorous manner. However, it is impossible to identify all safety concerns during clinical trials. Do you agree with that?
A Yes, I do.
Q Therefore post-marketing safety data collection and risk assessment based on observational data are critical for evaluating and characterizing a products risk profile and for making informed decisions

from risk minimization. Do you agree with that?
A Yeah, I believe that's from the FDA guidance document.
Q This guidance document focuses on pharmacovigilance activities in the post approval period. This guidance uses the term pharmacovigilance to mean all scientific and data gathering activities related to the detection, assessment, and understanding of adverse events. Do you agree with that?
A I use it a little differently, but that's fine. They define it within context.
Q Let me ask you a question: Do you know this document pretty well?
A Yes.
Q Is there anything in it that you disagree with?
A Some things, yes.
Q What do you disagree with?
A I mean, I can't say offhand.
Q Conceptually what do you agree with?
A It's a very good document and it's nice to have that, something that people can look at and refer to.
Q They talk a lot --
A I use it in my class.

Q They talk a lot about pharmacovigilance and the absence of data mining, correct, and even talk about how data mining is not required, correct?
A Yes, there's a statement in there about data mining is not a required part of pharmacovigilance.
Q Do you agree with that?
A Yes.
Q So signals can be found without data mining, correct?
A As a signal -- how are you going to define that in its context.
Q I mean, signal as in we have a real concern here, clinical meaning, everything?
A A clinical concern.
Q Clinical signal, a clinical concern that needs to be evaluated, followed-up, potentially lead to a labeling change. You don't have to have data mining for that?
A That's correct.
Q I think we talked about you don't have to have epidemiology for that either?
MR. BARNES: Objection.
A To work up the signal you would need to do epidemiology or experiments. You need to do something

to work it up.
Q But you don't have to -- you can make a labeling change before that, correct?
MR. BARNES: Objection. You're replowing old ground, Counsel.
Q I just want to clarify we're talking about a document. I want to clarify.
MR. BARNES: Why don't you show her the documents.
MR. ALTMAN: She knows the documents.
MR. BARNES: Well she said --
MR. ALTMAN: I'm not reading something from the documents, how can I refer to the documents?
THE WITNESS: I'm not going to make comments on the labeling changes. That's a whole different animal from this document.
BY MR. ALTMAN:
Q Do you know if there was anything that would have prevented the company from tuning its data collection practices in 1994 and 1995 when they first started getting post-marketing events for psychiatric conditions?
MR. BARNES: Objection. Assumes facts not in evidence. So if you can answer that go ahead.
A I'm not going to talk about their -- the

data collection process. I'm not privy to what they were doing.
Q I didn't ask you what they were doing. I asked you do you know of any technical reason they could not have had a specific protocol for collecting data related to the psychiatric adverse events in the 1994 timeframe?
A I don't know if they did or didn't or could or couldn't. I don't have an opinion on that.
Q You were doing -- dealing with drug safety issues back in 1994, correct?
A But not SOPs for data collection and pharmacovigilance, no.
Q Okay. I'll read you a couple statements and see if you agree or disagree with them. Because no pharmacologically active drug substance is entirely free of risk, the conclusion that a drug has been shown to be safe for use is actually no more than an opinion, albeit one offered by an individual reasonably knowledgeable in the management of that condition, that the intended target of treatment and the benefits associated with the use of the drug are sufficient to outweigh its known risks of use.
MR. BARNES: Objection. You read that very fast out and of context.

MR. ALTMAN: Do you want me to read it again?
MR. BARNES: Can you show her the document?
MR. ALTMAN: No.
MR. BARNES: Well, if you can't answer him reading from a document and out of context, just tell him that.
A I really would like that in context. It's kind of --
Q I'm just asking if you can't agree, disagree, that's fine.
MR. BARNES: Why don't you reread it.
Q I'll break it up. Because no pharmacologically active drug substance is entirely free of risk. Do you agree with that?
A Risk is, I mean, people drink too much water and have died from that.
Q I just asked do you agree that no pharmacologically active drug substance is entirely free of risk?
A Possibly, that's potentially true. Any chemical that one puts in one's body can have risks.
Q The conclusion that a drug has been shown to be safe for use is actually no more than an opinion. Do you agree with that?

A I disagree with that. It's an educated and informed evaluation. I don't believe it is purely an opinion.
Q It's still somebody's clinical judgment that that is in fact a true statement, correct?
A I don't believe it's one person's clinical judgment. I think it's -- it's much more than just an opinion. I think that really --
Q It's a clinical judgment of a group of people that conclude that that's true?
A Based on a wealth of information.
Q It's clinical judgment, though, correct? It's someone's judgment?
A Based on data.
Q It's still a judgment call, correct?
A The benefits? No, they're clearly identified in clinical trials.
Q That the benefits outweigh the risks?
A That is a process based on data.
Q And that's a judgment call, correct?
A But it's not just purely an opinion. A clinical judgment based on well controlled studies is much more than just an opinion.
Q That's fine. Accordingly, risk to benefit assessments are inherently arguable. Do you agree with

the drug be approved and the advisory committee doesn't agree with the FDA, correct?
MR. BARNES: If you know that.
A From my work it's very uncommon.
Q But it does happen, correct?
A I don't know when it's happened in recent history.
Q Does it go the other way around, too, sometimes some of the people at the FDA are not sure. There's some disagreement amongst the reviewers at the FDA as to whether the drug should be approved or not and the advisory committee is asked to take a look at everything and render an opinion?
A For approval decisions?
Q For approval. Well, for recommendation as to whether the drug should be approved. It's always up to the FDA, correct?
MR. BARNES: Say it again.
Q The final approval decision is always up the FDA, correct?
A That is correct. The FDA makes the regulatory decision to prove or disprove a drug.
Q And the advisory committee is brought in there to advise the FDA on what their opinion is, correct?

that?
A No. I believe they're within context.
Q So there's no -- so you've been on an advisory committee, is there not usually disagreement before a drug is approved or whether a drug should be approved or not?
A It varies.
Q But it's not rare that there's disagreement amongst members of an advisory committee, correct?
A Yes, I think it's more usual that there's agreement on the approval decision, but sometimes there can be disagreement.
Q So whether the benefits outweigh the risks is something that is reviewed and considered by the advisory committee, correct?
A When there's an advisory committee convened to do so, they would consider the benefits and risks.
Q And you sometimes have discussion and debate over whether the benefits outweigh the risks, correct?
A Sometimes. Sometimes there's discussion about what the risks are, what the benefits are. This is all -- discussion of all the points that are brought up.
Q And sometimes the FDA will recommend that

A If the FDA convenes an advisory committee they ask them specific questions. It's not always as straightforward as yes or no.
Q Understood.
A There's many questions they might ask.
Q Sometimes there's disagreement within the FDA. Within the clinical reviewers you may have some person -- some people say I don't think this should be approved and other people say I think it should be approved, it's okay with me. Correct?
MR. BARNES: Objection. Calls for speculation. If you know.
A I've seen in the newspaper a couple of cases, but I haven't heard that that is a normal circumstance at the FDA.
Q So in the couple of drugs that you approved, the FDA was all on board, everybody at the FDA was universally said this drug should be approved?
A Could you repeat that?
Q You were on the advisory committee to review a potential new drug application a couple times you said, correct?
A That's correct.
Q And those times the FDA made a presentation to the advisory committee, correct?

A Yes.
Q And the FDA gave its opinion on whether they thought the drug should be approved, correct?
A Not always.
Q But they looked to the advisory committee to render its opinion on whether the drug should be approved or not, correct?
A In some cases, yes.
Q Do you agree or disagree with the following: Given the average duration of randomized trials, often months to one or two years, and the average number of patients in randomized trials, often dozens to a few hundred, such trials are at most able to detect and quantify frequent adverse events that occur early only during treatment?
A Jerry Avore (phonetic).
Q No.
A No. Okay.
MR. BARNES: What's your question?
Q Do you agree with that statement?
MR. BARNES: Does she agree with that statement.
A Say it again.
Q Given the average duration of randomized trials, often months to one or two years, and the

Q Do you agree with that statement?
A As a general blanket statement, no, I have to have more context for that.
Q It follows that: Systematic reviews of drug treatments must include not only the results of randomized trials on benefits, but also evidence from observational research on harms. Do you agree with that statement?
A Say that again.
Q It follows that: Systematic reviews of drug treatments must include not only the results of randomized trials on benefits but also evidence from observational research on harms?
A I mean that's -- in what context, what reviews? I mean, meta-analysis?
MR. BARNES: If he doesn't give you enough information you can't answer.
A Yeah, I can't answer it.
Q That's fine.
MR. BARNES: If you show her the document you're reading from, it's a medical article.
Q That's okay.
MR. BARNES: Okay. If you can't answer, you can't answer.
Q If you can't answer it, you can't answer

average number of patients in randomized trials, often dozens to a few hundred, such trials are at most able to detect and quantify frequent adverse events that occur early only during treatment?
MR. BARNES: Objection.
A That's a very general statement. I think it would need to have a number of qualifiers in there.
Q Moreover, the adverse effect has to be known beforehand or anticipated to be recorded systematically in the trials?
A I don't agree with that statement.
Q The study population in trials which often includes young persons with a single diagnosis and without concurrent disease is often not representative of those who eventually use the drug in the community. Do you agree with that?
MR. BARNES: Objection.
A What's your question?
Q The study population in trials, which often includes young persons with a single diagnosis and without concurrent disease is often not representative of those who will eventually use the drug in the community?
MR. BARNES: For Neurontin or just generally?

it. It's totally fine.
In contrast data from routine medical practice may very well be used to investigate adverse effects of drugs. Adverse effects of new drugs are often unknown and unanticipated when those drugs enter the markets. Do you agree with that?
A These statements are so general that they could be true or not true given the correct context. So I don't want to speculate what they're trying to say.
Q That's fine. Do you agree with the following statement: Data mining processes are not able to account for inaccurate or missing data and if a signal is not detected, it is impossible to determine whether no ADE exists or the data are insufficient?
MR. BARNES: Reread that. It's late and it's --
Q Data mining processes are not able to account for inaccurate or missing data and if a signal is not detected is impossible to determine whether no ADE exists or the data are insufficient. Do you agree with that?
A Whether not as written, there's a problem with that sentence.
Q Do you agree with the following sentence:

A signal may consist of only a few case reports and not be statistically prominent and nevertheless herald a true adverse reaction?

A Yes, I agree with that.

Q Once a signal has been recognized and assessed, it needs to be followed how it evolves over time in the database. For example, as regards absolute numbers of cases, the statistical parameters, exposure to the drug and the persistence of the characteristics and consistency of the reports. Do you agree with that sentence?

A In what context?

Q In the context of signals and pharmacovigilance?

A Repeat it, please.

Q Once a signal has been recognized and assessed, it needs to be followed how it evolves over time in the database. For example, as regards absolute numbers of cases, the statistical parameters, exposure to the drug and the persistence of the characteristics and consistency of the reporting pattern.

MR. BARNES: And signal as she has defined it for the purpose of her report or a signal based upon another data collection? Is this data mining or observational or clinical?

whether it has clinical significance?

A There are and there should be, within the company and within the FDA, protocol beforehand on how one deals with statistical alerts from data mining and what the triage procedure would be.

Q Understood. Does there have to be some triage procedure?

MR. BARNES: At what time? As of today's standards? As of today or different times? You're talking about a period of time here that is long. So if it's as presently defined or as understood in 2001. I mean, it's a completely vague as to time.

MR. ALTMAN: I'm asking her opinion on that.

Q Whether an alert needs to be followed up? Does something need to be done with an alert or is it okay to simply ignore it?

MR. BARNES: Objection. She's testified that you don't even have to do -- you're not even required to do anything with an alert under your own premise.

MR. ALTMAN: You're messing up the question.

Q If you see an alert, is it acceptable to do nothing?

MR. ALTMAN: This is a signal.

MR. BARNES: Well, objection. Vague.

A Yeah, within the context, I'm not quite sure what you're talking about.

Q That's fine. Do you agree with spontaneous reporting has been designed as a system for hypothesis generation in the first place. As a rule for the study using the most appropriate and usually different method is needed to put the hypothesis to the test?

A Let's break it up. I agree with the first sentence. What's the second sentence.

Q As a rule further study using the most appropriate and usually different method used is needed to put the hypothesis to the test?

A I agree that if you see an alert, or clinically relevant signal, you need to follow-up with another method to test the hypothesis in almost every case.

Q I think one thing we never finally finished up this morning. And I think I asked you. If you observe an alert, under what conditions is it okay to do nothing with the alert. Can you give me some examples of when it would be okay?

A An alert is purely statistic.

Q Okay. Does an alert need to be evaluated

A In what context?

Q To do simply nothing. You observe an alert. You run some kind of data mining analysis, you come up with an alert as we have discussed.

A For me or you?

Q I'm not asking for me or you. A company --

A A company.

Q -- defines an alert.

A For their drug?

Q For their drug. Is it okay to do simply nothing?

A I don't know what their SOPs are or their legal requirements. Is the alert evaluated clinically immediately? Is it separate? So, I mean, it really would depend on what's going on.

Q Does some kind of evaluation need to take place on the alert to decide whether to go further?

A I believe that it needs some clinical evaluation to see if the alert is actually a signal or if it is something that uninterpretable or something that may not be relevant.

Q Okay. So something has to happen. You see an alert. You got to do something. You may conclude that it's not relevant, you may conclude it's uninterpretable, you may do something. But what's not

okay is run your data mining and simply put your stuff on the shelf --

MR. BARNES: If you have an opinion.

A I can't make an opinion like that because you're talking in general and things are evolving even as we speak on how data mining is best used.

So things are evolving now and that's a good question that I don't think we have been able to answer yet as an industry on how to deal with data mining.

Q For your -- when you access Q Scan, is that through a web site? Do you go into your log-in and you can run your analyses?

A That's correct.

Q And you can download some of that data or computations or whatever that it produces?

A It's an application. It has software on it to do statistics, that's all it is.

Q How is the output given to you?

A It depends on what you're looking at.

Q The first time you provided us some Excel spreadsheets of data that formed part of the basis of your report, do you recall that?

A I believe I gave you the raw counts that were used to calculate the PRRs, yes.

Q Did you generate charts similar to that when you did your analyses in your supplemental report?

A Did I for here? No.

Q For your supplemental report?

A No, I didn't. Raw data.

Q How did you actually -- the charts that are in your supplemental report, did those come straight from Q Scan or do you actually have to make those charts? I'm talking about ones on the PRR?

A Which -- give me an example, which one?

Q Your supplemental report. Let's take on page 22?

A Figure 1?

Q Figure 1, yes.

A So I get the statistic, the PRR statistic, and I put it in an Excel spreadsheet and I plotted it in Excel.

Q I mean, did you hand write that stuff from Q Scan or did you download a chart or something?

A I believe I downloaded a delimited file to a data file.

Q Do you still have those files?

A Probably not. They're raw files. I would just recalculate it.

Q Okay. Did you write out a formal protocol

when you did these analyses?

A I put the protocol in my report. So yes, I decided beforehand what I was going to do.

Q Do you know whether Dr. Blume did a similar thing before she had analyses run?

A Based on the number of tables and runs that you did that were available on the CD that I reviewed, I suspect not.

Q Do you know if Dr. Blume said to run all adverse event terms at all MedDra levels?

A That's what it looks like to me that was done.

Q Is there something wrong with doing that, running all adverse event terms on all MedDra levels?

A Depends on what context.

Q Well, in this context here you make the suggestion that -- frankly, I think you make the suggestion that there's something wrong with doing that.

If the practice is to run every single adverse event term that actually occurs at all four MedDra levels, is there something fundamentally wrong with doing every possible term and generating those data?

A But what you -- you can look at whatever

you want to look at. But what is the intent and if you're going to do statistical analysis, you have to predefine what is your threshold.

I don't think it's a legitimate exercise to do the analysis and then afterwards to say, okay, here's my cut off. I like this cut off because this gives me what I want. You have to define your cut off threshold, algorithm statistic ahead of time.

Q Do you know whether Dr. Blume did that or not?

A She mentioned nothing about any statistic, any threshold, any significance level. I saw nothing in any report.

Q But that doesn't mean that she didn't do that, correct?

MR. BARNES: Objection.

A If I saw nothing in all the pages of all of these reports that she put together, she didn't bother to mention that and she mentioned everything else, I would assume that she didn't do it.

Q Did you put your thresholds in here?

A Yes, I did.

Q Where are they? Is that what you used on page 21?

MR. BARNES: Take your time. Maybe in your

first report.
A That's what I'm looking at.
Q I'm looking at page 21 of your supplemental report.
A I'm looking at page 21 of my first report using the full data set as a background, I calculated accumulated series of proportional reporting rates with a threshold PRR of greater than 2 with a chi-squared greater than equal to 2 commonly cited --
THE COURT REPORTER: Say that again.
THE WITNESS: Can I just reference you where it is?
THE COURT REPORTER: Whatever you'd like.
THE WITNESS: This is the first report. Do you know what it's labeled?
MR. BARNES: I don't think he marked it an exhibit.
THE WITNESS: Okay. I apologize. In my original report on page 21 I state the criteria that I used to do my analysis. The threshold that I used.
BY MR. ALTMAN:
Q If somebody decides to monitor specific adverse event information going forward for some reason, is that still data -- would you still consider that to be data mining?

A It depends on how they're monitoring it.
Q If I want to -- if I decide that I'm concerned about a particular adverse event based on for whatever reason. I've done some review. I've made clinical judgment that these particular adverse events are of concern to me, and I want to monitor those going forward and see what I see. Do you still consider that to be data mining in terms of looking at particular adverse events going forward?
A Not necessarily.
Q So that's more of a data -- can we call that a data -- can we call that monitoring, I mean simply a directed monitoring?
A It's some form of post-marketing surveillance.
Q Do you have any opinion whether there was any information in the possession of the company in 1994 that said it should have suggested to the company that they should perform any kind of enhanced monitoring of any particular adverse events associated with the use of Neurontin?
A Based on my review of the clinical trials that they submit to the FDA and the epidemiological literature and the spontaneous reports, I don't see that at all.

Q I'm talking about in 1994 when the drug was first put on the market. You wouldn't have had spontaneous reports and you wouldn't have had epidemiologic data?
MR. BARNES: Objection. Asked and answered.
A Based on all the information I reviewed, even today, I do not see any signal, any signal of disproportional reporting, any statistical associations, even today. So I cannot imagine that there would be anything available into 1994 if there's nothing available even to this point after it's been used so extensively.
Q Once again, your opinion is limited to not involving somebody's clinical judgment that there is something that should be monitored, correct?
MR. BARNES: Objection. She stated several times what she's based her opinion on, so state it again.
A I relied on the clinical judgment of the experts that put together the reports, the Parson's report, the FDA analysis which had a number of clinical experts on it, the medical literature which has clinical experts writing paper.
So based on the preponderance of evidence

that I reviewed, the epidemiological literature and the clinical literature, I do not see any information even today that would make one believe or even suggest that there would be a statistical association with Neurontin and suicidality.
Q Just quickly, I have these invoices here. I'll mark these. This is the only copy. I guess we'll just mark it as an exhibit. I just want you to review this and see if these appear to be your invoices in this case?
MR. BARNES: Up through today or?
MR. ALTMAN: Up to today. I mean, those are the invoices I was handed. I have no basis of knowing anything else.
A These are the invoices from the last -- the deposition, the last deposition. It's not prior to that. Except for this one because they didn't pay until afterwards. So this is things received in 2008.
Q Let's mark that as the next exhibit.
(Whereupon, a document was marked as Deposition Exhibit Number 28.)
Q I guess we'll mark as -- these are the disks that you brought with you today?
A Yes, I brought those with me today.
Q Why don't we mark these as 29 through 32.

And I believe we are out of time much to your chagrin. I thank you for your time and I just want to put on the record that, once again, I did not have the opportunity to access Q Scan data. I don't know what that access would do in terms of my desire to ask questions of this witness and so under the MDL we're entitled to two days and under the California rules there's no time limit. And therefore I'll hold this deposition or I'll adjourn this deposition for now pending my review of that information which may require some further examination of this witness.

MR. BARNES: Okay. Well, I think what I would ask you to do is put your request -- precise request to us in writing and we will respond as to the Q Scan data, what your current request is and we'll are consider it and go from there.

MR. ALTMAN: That's good.

EXAMINATION BY MR. BARNES:

Q One question of the witness before we conclude. Very early in the deposition Mr. Altman asked you a question regarding the scientific rigor in which you prepared your report and you stated that you used the same, I'll paraphrase, it, the same scientific rigor that you would use in doing your other professional work except you didn't have as many hands

to look at the references, what did that mean?

A It means that this did not go through a formal peer review process. So if I write a paper, one, I'll have usually many co-authors. So everyone gets to review that and then I have a -- an editor in-house that will go through and edit. And then when I submit it to a journal for publication, it gets sent out to at least two, three, four peers that go through every aspect of the paper.

Q In that process from time to time do they find typos and errors within the draft manuscript?

A No matter how many times you write and rewrite it, there's always something, yes. They are noticed. Then also if it's accepted the journal has editorial staff that again go through it and sometimes you'll find them.

Q So that's the difference?

A And then proofs. There's many, many steps in the process to make sure.

Q So the error that Mr. Altman pointed out this afternoon is something that would perhaps come to light during the normal peer review and editing process that you do in your normal scientific and research activities, correct?

A Absolutely. Very minor typos or things

like that would be caught and corrected. Absolutely.

MR. BARNES: Thank you. No further questions.

EXAMINATION BY MR. ALTMAN:

Q I have to ask a brief follow-up. You don't know how many errors there are in either your supplemental report or your original report if you didn't go through that process, correct?

A I went and did this as thoroughly and as carefully as I could. I found errors in everybody's reports on this case, including a couple of typos on my own report.

Q But you don't know if there are other errors in your report, correct?

A I know there's a couple of typos.

Q I'm not talking typos, numerical errors?

MR. BARNES: She said that was a typo.

A I know there's some typos in it.

Q Is that --

A But, I mean, I am going to assume that there are not unless I find something. I've gone through and worked this very hard to make sure that this is accurate and correct.

Q Okay.

MR. BARNES: No further questions. Thank

you. We will read and sign.

(Whereupon, CD's were marked as Deposition Exhibit Numbers 29 through 32.)

(Deposition concluded at 6:30 p.m.)

CERTIFICATE OF DEPONENT

I hereby certify that I have read and examined the foregoing transcript, and the same is a true and accurate record of the testimony given by me.

Any additions or corrections that I feel are necessary, I will attach on a separate sheet of paper to the original transcript.

_____

SHEILA WEISS SMITH, Ph.D.

State of Maryland,
County of Baltimore, to wit:

I, RONDA J. THOMAS, a Notary Public of the State of Maryland, Baltimore County, do hereby certify that the within-named witness personally appeared before me at the time and place herein set out, and after having been duly sworn by me, according to law, was examined by counsel.

I further certify that the examination was recorded stenographically by me and this transcript is a true record of the proceedings.

I further certify that I am not of counsel to any of the parties, nor in any way interested in the outcome of this action.

As witness my hand and notarial seal this 5th day of January, 2009.

_____

RONDA J. THOMAS
Notary Public

My Commission Expires:
October 1, 2009